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RECENT ADVANCES IN CARDIOVASCULAR DIAGNOSIS AND TREATMENT

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I take great pleasure today in bringing the wartime greetings of the medical profession of Massachusetts and of New England to the medical profession of North Carolina at this, your annual meeting, and, in particular, the greetings of the Massachusetts General Hospital to Charlotte. On an early spring day twenty-four years ago in a little village in southwestern France during another war a small but sturdy group of thirteen officers, twenty-one nurses, and forty-five enlisted men of Unit O from Dixie joined for the duration U. S. Base Hospital No. 6, composed of Yankees. During that next year there were cemented close friendships which have ripened with the years that have passed. My visit to you today is in large part the result of that chance occurrence in March, 1918.

And now for the particular subject of the day—"Recent Advances in Cardiovascular Diagnosis and Treatment".

"Yet, even since the times of Corvisart and Laennec there has been a great advance in our knowledge of cardiac and arterial disease; and, in proof of this assertion, it is only necessary to refer to the many works of a formal nature, and again to the numerous and equally valuable class of monographs which have been produced on these subjects during the last few years." These words sound very modern, but they were actually written by William Stokes in 1854[1].

One hundred years before that, Senac in his TRAITE DE LA STRUCTURE DU COEUR, DE SON ACTION, ET DE SES MALADIES[2], wrote: "The brain is not sufficiently large and life is too short to embrace all anatomy. In spite of all the help which our predecessors have given to us, it is hardly possible for a man to develop with exactness knowledge of a single organ. Those long works which mention the details of each part of the body proclaim their own sterility even by their extent. They are like geographic maps of the entire world. The kingdoms appear only as dots."

And Latham in 1845[3] wrote: "The study of our times has been chiefly to specialise and to localise disease, and it has had very useful results. But it has had a tendency to narrow our views, and to cripple our practice, by setting up as many several pathologies within the body as there are several organs. Yet no sooner do the diseases of separate parts come to be treated, than they begin to claim their place in a common pathology."

The increase in our knowledge of cardiovascular disease had a very slow beginning several hundred years ago, getting off to a fairly good start at last in the years just before and just after 1700, and building up gradually through the eighteenth and nineteenth centuries until it received its present impetus a generation ago through the stimulus of such men as Mackenzie and Wenckebach and their many pupils. Since the first

Read before the Second General Session, Medical Society of the State of North Carolina, Charlotte, May 13, 1942.

1. Stokes, William: The Diseases of the Heart and Aorta, Dublin, Hodges and Smith, 1854.
2. Senac: Traite de la Structure du Coeur, de son Action, et de ses Maladies, Paris, Briasson, 1749.
3. Latham: Lectures on Subjects Connected with Clinical Medicine, Comprising Diseases of the Heart, London, Longman, Brown, Green, and Longmans, 1845.

World War the pace has been fast, and much has been learned in the last two decades, largely because of the concentration in this field by many workers all over the world. It is a pity that there must be some pause in this important work now in the present world conflict, but it is first essential to free the world from the menace of such very interruptions as this.

I shall discuss briefly this afternoon recent progress in diagnosis, present a few diagnostic clues that have become clarified in the last decade or two, and close with some remarks about treatment.

Cardiovascular Diagnosis

First and foremost should be mentioned what I believe to be the most important problem of all, but the one which has been the most neglected and which is only now exciting our attention—namely, *the range of the normal heart.* Like other organs and systems in the body, the heart and circulation in disease have always interested the doctor more than the heart and circulation in health, and the physiologist, though he has analyzed the various functions and activities of the cardiovascular apparatus, has not taught us the normal range. Gradually, in the last few years especially, it has dawned upon us that the range of the normal heart in man is exceedingly wide, in its size and shape, rate and rhythm, force and endurance, and in its blood pressure, x-ray shadow, and electrocardiogram. We do not know as yet the bounds of the normal heart, but we have learned that a good many findings which were once considered evidence of disease are actually normal enough for the particular type of human individual concerned. This knowledge is of the greatest importance, not only in avoiding the label of disease when there is none, but also in allowing these normal individuals to be accepted for various activities, such as military service, a vital need of the moment. For continuation of this study, better correlation with body build and constitution is needed than our present knowledge will permit. For example, the best measurements of heart size at present available—namely, the Hodges Eyster nomograms for the predicted normal size of the area and transverse diameter of the x-ray heart shadow—allow too great a range of variation (from plus 10 per cent to minus 10 per cent) to be of any great value; the hearts whose size is clinically questionable remain for the most part questionable even after careful and elaborate mensuration. Startling discoveries have been made of the range of the normal electrocardiogram, as in Graybiel's series of records from 1,000 healthy aviators.

Next in importance comes the *incidence of heart disease and of its types* throughout the world. A few statistical data of some interest have been collected of late in this country, but that is but a small beginning. A wealth of information of great value awaits us. We cannot experiment adequately on man, nor can we translate to man animal experiments in this field with any degree of certainty; but nature has been carrying on human experiments, some simple, others complicated, in all parts of every continent and over the seven seas. How do climate, food, physical activities, racial stock, habits, and disease affect the heart and circulation in various different communities the world over? We should get at this problem when the war is finished.

Now let me take up the different kinds of heart and blood vessel diseases, beginning at birth. More advance has been made in the recognition of *congenital defects* than in any other type of cardiovascular disorder in the last decade or more. Prognosis, and now even treatment since the introduction of ligation of the patent ductus arteriosus, depend largely on the particular structural lesion present. We have come to recognize certain defects which were scarcely mentioned in my medical school days: a few of these are coarctation of the aorta, auricular septal defect, the tetralogy of Fallot, and the right aortic arch.

Rheumatic heart disease has become more clearly understood, although its exact pathogenesis is still unknown. We now appreciate its dependence on infection by the hemolytic streptococcus, and thereby its climatic variation, the common acute or subacute myocardial involvement with not infrequent reversible dilatation of both ventricles, the good prognosis and extended longevity in many cases, and its decrease with improvement in living conditions in any community.

Hypertensive heart disease is better understood, consisting as it does of left ventricular enlargement from the strain of systemic hypertension of any sort—most commonly, of course, from the so-called essential hypertension, still a mystery on the eve of solution. I should like to emphasize,

however, that in many persons the blood pressure never stays high enough long enough to cause any heart disease. Hypertension is not synonymous with hypertensive heart disease.

There is another type of hypertensive heart disease, generally acute, that has been largely explained in the past decade—namely the *cor pulmonale*. Increase of pulmonary blood pressure, if extreme, can cause dilatation and even failure of the right ventricle. In acute form it may arise from massive pulmonary embolism, and has been labeled the *acute cor pulmonale*. This can give rise to a characteristic electrocardiographic pattern; it is to be noted, however, that in at least 90 per cent of the cases pulmonary embolism is too slight or is too rapidly fatal (by vascular shock) to produce the clinical and electrocardiographic picture of the acute cor pulmonale. The acute dilatation can go on to a chronic state, which, however, in high degree is rare and then is best recognized electrocardiographically. Lesser and unimportant cor pulmonale occasionally may occur from pulmonary fibrosis due to serious chronic pulmonary infection or silicosis, but failure of the chronic cor pulmonale is extremely uncommon.

Here for a moment I should like to digress to speak of that very important vascular accident, *pulmonary embolism*, which frequently causes death by shock and occasionally affects the right ventricle, as I have just said. This condition is common medically as well as surgically, but in medical cases has been largely overlooked in the past and still is recorded as rare in many places, being called pneumonia, pleurisy, lung congestion from heart failure, or even coronary thrombosis. It is to be noted that recurrent pulmonary embolism is especially common in cardiac patients, particularly in those in congestive failure, in whom it is actually the most common cause of death. There are three reasons for the failure to recognize it clinically more often: (1) it is not thought of, (2) it is often concealed by the signs of congestive failure, and (3) it does not usually give rise to the old text book picture with blood spitting. An otherwise unexplained episode of chest discomfort, of acute breathlessness or pulmonary edema, of tachycardia, cyanosis, fever, or leukocytosis, alone or in various combinations, should make one think of the possibility of pulmonary embolism, especially if it is repeated in a cardiac patient or in a person who has sprained an ankle or had some other leg injury. Pleural pain or friction rub, blood spitting, x-ray evidence, or the acute cor pulmonale electrocardiogram are, of course, if present, very helpful in confirmation. But the most important point in making the diagnosis of pulmonary embolism early is to search for what is almost invariably the fundamental cause and to correct it, thereby occasionally saving a life. Infrequently is the heart the source of the embolus. It is usually one of the long leg veins that is at fault, even though careful examination may not reveal it. Frequently by the time the leg swells or is painful or tender the danger is over and the other leg may then be the focal hazard. Therefore, if in doubt one should obtain a *venogram* of each leg—that is, an x-ray picture of the deep and superficial veins by diodrast injection. Careful technique and experienced interpretation are essential, but when it is clearly evident that the long veins are affected, their ligation should be carried out at once.

Let us turn now to one of the most fascinating forward steps of all—namely the appraisal of *coronary heart disease*: angina pectoris and coronary thrombosis. Once upon a time, not much more than ten years ago, these conditions were viewed with great pessimism. It was thought that chronic invalidism and sudden death in the not far distant future were the natural results. Clinical and autopsy experience, and certain researches, especially those of Schlesinger and Blumgart, have radically changed our viewpoint. Now we realize that only about 10 per cent of patients with coronary heart disease come to grief quickly; that a great many patients live for a good many years only slightly or occasionally bothered by coronary insufficiency; and that an appreciable number, probably 10 per cent or more, recover completely to resume a normal life and are likely to die in old age of something other than heart disease. This advance has come through the careful follow-up study, with autopsy, of many individual patients, the widespread introduction of electrocardiography, and the demonstration of the frequency with which adequate collateral coronary circulation is established in affected hearts. A corollary is that coronary disease is not synonymous with coronary heart disease; indeed one or more of the main coronary arterial trunks may be completely

occluded (by a slow process) with never any symptoms of myocardial injury. Undoubtedly the large increase in cases diagnosed as coronary heart disease is due in great part to recognition in our times of the lesser degrees of the disease.

Acute and chronic constrictive pericarditis has also come into prominence in the last dozen years or so. The clinical recognition of the acute cases presenting tamponade by effusion or hemorrhage was made occasionally in former days, but is now common. Proof is furnished by increase in the bulk of the heart and pericardial sac, plus small arterial pulse pressure, paradoxical pulse, and increased systemic venous pressure (engorged neck veins and liver). Paracentesis or operation can save such patients. The chronically constricted heart likewise shows a low arterial pulse pressure with engorged neck veins and liver, but there are also findings of ascites, a heart of normal size or only slightly enlarged, often no murmurs, but a loud third sound, always an abnormal electrocardiogram (flat or inverted T waves and often low voltage of the QRS waves), and sometimes calcification of the pericardium demonstrated by x-ray. Recognition of this condition is vital, since cure is possible in about half the cases by operation, consisting of pericardial resection.

Two aortic diseases in particular I should like to mention, also newly recognized clinically in recent years. These are dissection of the wall—the so-called *dissecting aortic aneurysm*—, and *arteriosclerotic aneurysm*, both in contrast to the usual luetic aneurysm. A hypertensive patient may suffer a sudden excruciating pain in the thorax, radiating down the back, which is due to the splitting of the aortic wall; the differentiation of this vascular accident from coronary thrombosis is important largely because of its serious prognosis (90 per cent or more fatality). That old persons can die of rupture of arteriosclerotic aortic aneurysms, usually abdominal but sometimes thoracic, should be clearly recognized; to call all aortic aneurysms luetic is to do two possible wrongs: first, to attach to the patient a stigma that is unjustified, and second, to subject him or her to quite unnecessary and sometimes harmful anti-luetic therapy.

Finally, there have been recognized in recent years a wide variety of *rare cardiovascular diseases* important only because they should be thought of in obscure or doubtful cases. They include such conditions as Fiedler's myocarditis, sarcoid disease, amyloid disease, glycogen storage (von Gierke's) disease, disseminated lupus, periarteritis nodosa, avitaminosis, and cardiac enlargement and failure due to paroxysmal tachycardia at excessive heart rates. Altogether these conditions comprise less than 1 per cent of all cardiac cases.

Before turning to certain diagnostic clues I would add a few words about advances in *differential diagnosis* and in the use of roentgenology, electrocardiography, and other methods of study. We have learned to distinguish more clearly than we once did between *cardiac and gastrointestinal symptoms*, and more particularly between angina pectoris and cardiospasm or esophageal spasm (often due to hiatus hernia); and between coronary thrombosis or myocardial infarction and gallbladder disease. Perhaps the most important lesson that we have learned in this relationship or differentiation is that cardiac and gastrointestinal conditions can and frequently do occur together. We are also now on the watch to distinguish between *acute myocardial infarction and pulmonary embolism* and between *acute myocardial infarction and acute pleuropericarditis.* We must not confuse the electrocardiograms of *coronary heart disease and myxedema.* We must differentiate between *left ventricular failure and pulmonary emphysema or infarction* and between *right ventricular failure and constrictive pericarditis or local venous stasis.*

Roentgenology has made possible great strides in cardiovascular diagnosis, particularly in demonstrating the characteristic heart shapes of certain congenital defects, the size and extent of pulsation of the pulmonary blood vessels and of the aorta, the size of the left auricle, and calcification of the pericardium, valves and coronaries; but it has serious limitations, as I have already pointed out, in not demonstrating clearly slight cardiac enlargement when it is most important to recognize it, and in occasionally showing a normal heart shadow when other clear evidence of heart disease is present. However, with full recognition of its limitations, we should employ roentgenology, especially fluoroscopy, in checking our histories and physical examination. One of the important errors in interpretation still current is the inclusion of the triangle of pericardial-diaphragmatic fat as a part

of the heart shadow, thereby causing a false diagnosis of cardiac enlargement to be made. The use of diodrast delineation of the great vessels and heart chambers in expert hands has been a great step forward in the solution of obscure diagnostic problems, as has been also the outline of the peripheral vessels in appropriate cases, especially the venograms in suspected instances of phlebothrombosis. Kymography, tomography or laminagraphy, and cinematography have yielded less valuable information.

Electrocardiography has proved of greater value than roentgenology of the heart in cardiac diagnosis, but it too must be evaluated with special care. Heart disease is at present overdiagnosed as the result of its use. It is of most value in revealing or confirming coronary heart disease and preponderant enlargement of one or the other ventricle, in elucidating arrhythmias, and in helping to solve obscure cases. The chief advance in recent years in electrocardiography besides the realization of the wide range of the normal has been in the application of the chest or precordial leads. Our knowledge of these leads is still in a state of flux, but their chief value is in revealing and localizing myocardial disease of any type, but especially that due to coronary disease since that is the most common. It is now evident that chest leads are not necessary in the majority of cases; that when they are used, multiple leads are wisest, especially from lead points C_1, C_3, and C_5; and that accuracy in technique and interpretation are essential, for otherwise they do more harm than good. A progress report will shortly be published on this difficult subject by the Precordial Lead Committee of the American Heart Association.

Other laboratory tests, such as those of circulation rate, venous pressure, and blood gas content, are relatively unimportant for routine use although they have been helpful in research to elucidate certain circulatory problems and are useful in rare problem cases.

Diagnostic Clues

The most important advances in diagnosis have really been in the better recognition and the more intensive and widespread utilization of the clinical significance of simple symptoms and signs, findings that require the use merely—though to be sure the skilled use—of eyes and ears, fingers and brain. I would like to mention now some examples of such helpful diagnostic clues that have become better appreciated in recent years.

A. *Pain.*

1. *The angina pectoris of coronary insufficiency.* Of prime importance is the circumstance of its occurrence. Of less importance, but nevertheless very helpful, are its character (a tightness, waxing and continuous, though brief), its short duration, its location (substernal as a rule), and its quick relief by nitroglycerine. It is rare in women under 50 but common in men after 40.

2. *Prolonged heart pain aggravated by deep inspiration* means acute pleuropericarditis.

3. *Abrupt excruciating pain radiating down the back* suggests a dissecting aortic aneurysm.

4. *Tenderness accompanying heart pain* minimizes its importance.

5. *Tachycardia may cause pain* due to coronary insufficiency or to nervous discomfort.

6. *Right upper quadrant pain on effort* (due to liver congestion) in mitral stenosis or in other strain on the right ventricle is the first symptom of right ventricular failure.

7. *Substernal discomfort* when the patient is seated or recumbent and not on effort is not due to coronary insufficiency; it is most likely of gastric origin due to cardiospasm, quite commonly from a hiatus hernia.

B. *Dyspnea.*

1. *It is non-cardiac if the heart is normal in size.* It is most commonly of pulmonary origin or asthmatic.

2. *Sighing respiration* is a nervous, not a cardiac symptom.

3. *Cheyne-Stokes respiration* when the subject is awake is a serious sign of circulatory failure.

4. *Paroxysmal dyspnea* in a case of left ventricular strain is serious, but not as serious in mitral stenosis. In the former it is evidence of myocardial failure; in the latter it is merely a mechanical fault.

5. *Recurrent dyspnea with tachycardia and fever* with or without heart failure suggests pulmonary embolism.

C. *Palpitation.*

1. *Per se this is unimportant* if there is no other evidence of heart trouble, though it is often disagreeable. It includes not only extrasystoles and paroxysmal tachycardia,

but *also auricular fibrillation and flutter.*

2. *Tachycardia,* no matter what the rhythm, may precipitate coronary insufficiency, myocardial insufficiency, or psychoneurosis.

3. *Difficulty in controlling heart rate,* especially in auricular fibrillation, by rest and digitalis, means either nervousness, thyrotoxicosis, infection, or infarction (especially pulmonary).

Signs.

A. *Cyanosis.* This is more often pulmonary than cardiac in origin, even in a heart failure patient. It must be distinguished from argyria and polycythemia.

B. *Jaundice* in congestive failure suggests a large pulmonary infarct.

C. A *big heart* is evidence of chronic heart disease as a rule, but there is such a thing as reversible acute dilatation, especially in acute rheumatic myocardial involvement, acute cor pulmonale, and very severe paroxysmal tachycardia (in infants especially).

D. *Heart sounds.* Pulmonary second sound markedly accentuated in hypertension is important evidence of left ventricular failure, and in congenital heart disease of an auricular septal defect. Gallop rhythm at the apex and lower end of the sternum is usually a sign of serious ventricular dilatation (left and right respectively).

E. *Murmurs.* A harsh systolic murmur at the apex, heard also at the aortic area but not in the lung bases, usually means aortic stenosis; more blowing in character and heard also at lung bases but not in the aortic area, it means mitral regurgitation. In the interpretation of a continuous murmur a venous hum in or transmitted from the neck must be ruled out. Delicate aortic and mitral diastolic murmurs vary in audibility with body position, stethoscopic chest piece, and exercise.

F. *Pulse.* Great difference in volume of wrist pulses suggests aneurysm. Well marked pulsus paradoxus favors acute or chronic constrictive pericarditis. One must exclude compression of subclavian arteries on raising shoulders in deep inspiration. True pulsus alternans means serious left ventricular weakness, except in cases of excessive paroxysmal tachycardia. Absence of pulse in the feet points most often to local occlusive arterial (especially Buerger's) disease, but in rare cases to arterial embolism, dissecting aortic aneurysm, or coarctation of the aorta. Do not confuse the deep systolic jugular pulse with the carotid pulse.

G. *A systolic thrill palpable over the aortic valve area* almost always means aortic stenosis, rarely aneurysm; *a systolic thrill at the left border of the sternum* means as a rule a congenital ventricular septal defect.

H. *Left vs. right hydrothorax in heart disease.* The former, if isolated or preponderant, is more often due to pulmonary infarction or pleurisy than to congestive heart failure. Polyserositis must be distinguished from dropsy.

I. The same statement applies to the finding of *rales at the lung bases*—that is, pulmonary infection or infarction, or even atelectasis, is the commoner cause.

J. *Exclusive or preponderant unilateral leg edema* means local trouble, even in heart failure, provided the *effect of gravity* (lying on one side) *is ruled out.* Often this sign is due to phlebothrombosis, which may lead to pulmonary embolism.

K. *Engorged neck veins* almost always mean right heart failure, rarely acute or chronic constrictive pericarditis or pressure from a tumor; they always indicate the presence of a big liver too.

L. *A big liver without increased neck veins* (and venous pressure) means a noncardiac cause (cirrhosis - early stage -, hepatitis, tumor, etc.); the liver edge is unreliable as an indication of the size of the liver.

Treatment

"Many think that the expectation of effecting an improvement in the treatment of diseases of the heart, is chimerical; and they think so because, not being accustomed to recognize the diseases in question before they have attained an advanced stage, they are pre-occupied with the old and popular idea of their incurability. To such it might, perhaps, be a sufficiently philosophical answer to reply, that an improved knowledge of the nature and causes of a disease, must alone necessarily lead to an improvement in the treatment; and that therapeutic weapons are dangerous when wielded in the dark. But here we may go much farther: we may say that, by the improved means of diagnosis, the maladies under consideration may be recognized, not only in their advanced, but in their incipient stages, and

even when so slight as to constitute little more than a tendency . . .

"Thus it is seen that the practical improvements to be derived from a better knowledge of the diseases of the heart, extend, not to the diseases of this organ alone, but to a multitude of the most formidable maladies incident to the human frame. There is, in short, scarcely an affection with which disease of the heart may not be more or less interwoven; and, 'if,' to use the language of Senac, 'we would not pronounce rashly on an infinity of cases; if we would not harass our patients by noxious and unavailing remedies; if we would not accelerate death by treating certain diseases like others which are entirely different; nor be exposed to the disgrace of seeing our diagnosis falsified by the results of dissection; finally, if we would not have danger to be imminent, whilst we are under the blind impression that it is remote, we must study the diseases of the heart.' "

So said Hope one hundred and ten years ago[4].

There are a few particular points about the evaluation of the treatment of heart disease that I shall emphasize now in closing. In the first place, I cannot too strongly reiterate that there is a natural tendency for recovery in three particular cardiac conditions—namely, acute rheumatic heart disease, acute coronary heart disease, and congestive failure set off by tachycardia, pulmonary embolism, or infection. No matter what we do, patients with these conditions are likely to recover, but, of course, rest and specific measures are helpful. By specific measures, I refer to sedatives and narcotics when necessary, oxygen, digitalis, and diuretics. Too much credit has been given to various drugs and surgical measures for recovery from these conditions, when recovery would have occurred anyway. I do not want to be regarded as a therapeutic nihilist, but twenty-five years of experience with these particular cardiovascular troubles have convinced me of the truth of the remarks that I have just made.

In the next place, I need hardly mention what has been a great advance in the last decade or two in cardiovascular therapy—namely, the introduction of the mercurial and other diuretics to supplement the effect of digitalis in congestive heart failure. At first there was a good deal of fear that the mercurials might have a harmful effect on the kidneys, but it is astonishing how rare has been any such harmful effect; without doubt many lives have been prolonged and made much more comfortable by the free use of diuretics when needed.

Chemotherapy in subacute bacterial endocarditis, particularly the use of the sulfonamides and especially sulfapyridine, has improved the formerly hopeless outlook in this dread disease. In a review by Kelson and myself[5] of 250 well authenticated cases of subacute bacterial endocarditis studied in the Boston hospitals between 1927 and 1939, there was only one recovery, and that was for but a year. Since 1939, the mortality has been reduced, at least in our experience, so that now between 5 and 10 per cent of the patients recover. This is not a great reduction but it is well worth while. Whether or not heparin and other measures such as hyperthermia are important adjuncts remains for the future to decide. Heparin has the best rating so far and is not as dangerous as many have thought it to be.

Surgery has been responsible for definite advances in cardiovascular therapy, the most striking of which has been the cure of some 50 per cent of patients with chronic constrictive pericarditis by pericardial resection in the hands of expert and experienced surgeons. As I have stated earlier, it is vital to recognize clinically this uncommon but important condition. A further advance of great interest and also of value was made by Gross of Boston, who has ligated the patent ductus arteriosus in young people when there is definite evidence of important strain on the heart by this congenital defect. Another surgical measure which I have already spoken of but which I cannot emphasize enough is the ligation of thrombosed leg veins responsible for recurrent attacks of pulmonary embolism, any one of which can be fatal. Splanchnic resection in hypertension has been at times disappointing, but there is a small group of patients that have been spectacularly relieved. General treatment of hypertension remains inadequate, however, and we are looking forward hopefully to the day when there may be a specific extract or drug that can take care of hypertension and thereby ward off the serious

4. Hope: A Treatise on the Diseases of the Heart and Great Vessels, Comprising a New View of the Physiology of the Heart's Action, London, William Kidd, 1832.

5. Kelson, S., and White, P. D.: An Analysis of Two Hundred and Fifty Cases of Subacute Bacterial Endocarditis, To be published.

effects of chronic severe hypertension on the heart, arteries, and kidneys.

Preventive measures have already had spectacular success in two cardiovascular conditions that used to be serious. One is luetic aortitis, which now by the prevention or early and adequate treatment of syphilis has become rare in the most progressive communities. The other condition which we used to see a generation ago—namely, thyrotoxic heart disease—is now in advanced communities almost unknown. Further preventive medicine can be practiced in cutting down various factors of strain in the presence of organic heart disease. Too little attention has been paid to this matter, and yet it remains one of the most important reasons why the early diagnosis of heart disease is worth while long before heart failure comes.

Finally, I want to emphasize the value of reasoned optimism in treatment. One can thereby often avoid cardiac neurosis, whether there is any heart disease or not.

Summary

History has shown that the whole world—not just one school or city or country—has made steady advance in our knowledge of cardiovascular disease. It is quite certain that such advances will again be made universally. For the time being, however, it is of prime importance to finish this present world war, so that we may avoid in the future such interruptions of scientific advance as have resulted both from the present war and from the first World War. In ending, I would once more quote from the preface of Senac's TREATISE ON THE HEART[2], written two hundred years ago: "I have tried to avoid that prejudice of nationalism which dominates even the scientist. Several imagine that genius and knowledge are attached to their countries alone and that other nations are condemned by nature to sterility. This vanity may perhaps be useful to certain states; in inspiring confidence and scorn it inspires courage or ferocity but it degrades the mind. Genius is the prerogative of no nation. It is sown by chance amidst stupidity and ignorance. Let men who have the spark in common be separated by the seas or by long stretches of land and yet they form a spiritual republic.

"It is not sufficient to study the works of so many writers who have examined the heart. I have consulted this machine itself in order to discover that which has escaped them. I had thought at first that one could add nothing to their researches but one knows only gross facts about this organ and even these are not accurately described. To develop them I have searched in its very tissue. Such is the fertility of nature that it presents, to all, objects which one does not seek and findings that one has not foreseen."

THE STRUCTURAL BASIS OF PSYCHIATRY

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PHILADELPHIA

It is possible that the mere title of my paper will, in these days of emphasis on the psychogenic, arouse passive resistance in some of my listeners. Moreover, the lack of proof available for some of its concepts may arouse more active resistance. It seems desirable nevertheless to attempt to assess some of the structural background against which psychodynamic mechanisms operate, and to indicate some of the structural damage which may follow too enthusiastic application of some of our newer methods of treatment. An attempted assessment of structural mechanisms in psychiatry may be of value, if only to emphasize the fact that the brain still remains the organ of mind.

Organic Versus Psychogenic

Before proceeding to a consideration of the main problems of my discussion, let me first direct attention to the "either/or" concept which has dominated psychiatry for too long. I refer of course to the fact that processes in the psychiatric field are regarded as either structural, usually referred to as organic, or psychogenic, erroneously spoken of as functional. The schism, I presume, has been fostered by the rise of purely psychogenic concepts in psychiatry and by the meager contributions of the purely structural fields to an understanding of psychogenic mechanisms. Despite the description of the brain changes in psychiatric disease —for example, in general paresis, alcoholism, and trauma—, neurology has failed to clarify the purely non-structural or intangible aspects of psychoses or neuroses. The

From the Department of Neurology, Jefferson Medical College.

Read before the North Carolina Neurologic and Psychiatric Association, Charlotte, March 27, 1942.

disorders of emotion and mind, the personality problems all remain unsolved. Structural damage in itself can explain little unless there is correlation between damage and response. The concept has developed therefore that structural neurology has nothing to offer in the understanding of the emotions, of human motivations, or of personality disorders, and it has become customary to speak of the structural or organic as something wholly apart from the purely psychogenic. That this concept has proven unsatisfactory to most psychiatrists is attested by the recent healthy revival of psychosomatic medicine, which represents merely a rebirth of the unitary concept of body and mind.

The controversy between the structural and psychogenic approaches is an old one, and usually appears in the guise of identity or separation of body and mind. I have no desire to discuss this purely metaphysical aspect of psychiatry, and indeed am not qualified to do so. But I regard it as vital to the interests of psychiatry to analyze the separate contributions of both the structural and the psychogenic approaches and to discover how both work in unison. For it seems to be indubitable that the one is dependent on the other, and that without a brain or spinal cord all our psychogenic mechanisms have little meaning. If it cannot be shown conclusively how the brain integrates impressions to produce experience, it can at least be demonstrated that decortication eradicates much that is essential in human living.

Structural Basis of the Emotions

It is important to know how the emotions operate in the physical mechanism, and in recent years much work has been done on this problem. Most of our attention has been focused on the hypothalamus, which appears to assume great significance in the problem of the emotions. It must not be forgotten, however, that other brain regions are also involved in the problem.

There are two main approaches to the structural background of the emotions. One has to do with emotional expression; the other with that less tangible feature, the affective aspect of emotions. Let us consider first the problem of emotional expression.

Expression of the Emotions. I shall direct attention first to the hypothalamic region, not because it alone is concerned in the problem, but because there is good reason to believe that it serves as a focal point for impulses received from other parts of the nervous system, and hence assumes unusual importance. That other parts of the brain are also essential is undoubtedly true, as will appear later.

1. *Role of the Hypothalamus.* Removal of the brain above the hypothalamus results in what has been described as "sham rage", a term coined in order to indicate that the rage reaction elicited in animals so treated is not associated with the affective disturbance itself, but only with the expression of rage reactions. The rage so evoked is undirected, never outlasts the stimulus, and responds variably, being elicited with ease in some cases, and with difficulty in others. It is characterized in experimental cats by such actions as lashing of the tail, arching of the trunk, thrusting and jerking of the limbs fastened to the animal board, protrusion of the claws and clawing movements, snarling, attempts to bite, panting, and movements of the tongue to and fro, and is associated with signs of sympathetic activity such as erection of the tail hairs, sweating, dilatation of the pupil, tachycardia and elevation of the blood pressure, and secretion of adrenin.

Indications that some lower center is involved in these fits of sham rage was first given by observations on decorticate dogs and cats. Such animals were found to develop rage reactions, as shown by the observations of Goltz[1], Rothmann,[2], Schaltenbrand and Cobb[3], and Dusser de Barenne[4]. It seemed from these experiments that removal of the cortex permitted free play to some other area normally held in check by the cortex. Since the reaction could not be elicited in the decerebrate animal with mesencephalic section, areas at a higher level were sought. In a series of experiments Bard[5] demonstrated that "the discharge of nervous impulses which evokes this extraordinary motor activity . . . . is conditioned

1. Goltz, F.: Der Hund ohne Grosshirn, Pflueger's Arch. f. d. ges. Physiol. 51:370-614, 1892.
2. Rothmann H.: Zusammenfassender Bericht ueber den Rothmannschen grosshirnlosen Hund nach Klinscher und anatomischer Nutersuchungen, Ztschr. f. d. ges. Neurol u. Psychiat. 87:247-313, 1923.
3. Schaltenbrand, G. and Cobb, S.: Clinical and Anatomical Studies on Two Cats Without Neocortex, Brain, 53:449-488 (Jan.) 1931.
4. Dusser de Barenne, J. G.: Recherches experimentales sur les fonctions du systeme nerveux central, faites en particullier sur deux chats dont le neopalium a ete enleve, Arch. neerl. Physiol. 4:31-123, 1920.
5. Bard, P.: A Diencephalic Mechanism for the Expression of Rage With Special Reference to the Sympathetic Nervous System, Am. J. Physiol 84:490-515 (April) 1928.

by central mechanisms which lie within an area comprising the caudal half of the hypothalamus and the most ventral and most caudal fractions of the corresponding segment of the thalamus . . . . Anatomical considerations make it improbable that the small remnants of certain thalamic nuclei left in some of the active animals were of any functional significance. Consequently it may be stated with assurance that the sham rage depends on the caudal hypothalamus." Moreover, Kessler[6] has shown that when the hypothalamus is not functioning there can be no spontaneous emotional display and stupor supervenes, while partial lesions of the hypothalamus or ventral portion of the thalamus seem to produce an unusual lability of emotional display.

The data accumulated by ablation experiments have been confirmed in stimulation experiments of the hypothalamic region. Electrical stimulation of the hypothalamus of cats by Ranson[7] and his co-workers elicited sham rage responses. "At the onset of stimulation the animal became alert, raising its head and opening its eyes, disclosing dilated pupils. The respiration increased in rate and depth, and the animal soon began to struggle, clawing, biting, and trying to free itself from the hammock in which it was restrained. If the stimulus was continued the hair on the back and tail began to bristle, sweat appeared on the pads of the feet, and saliva ran from the mouth . . . . In all these respects the cats behaved as they would had they been threatened by a barking dog. The reactions were specifically hypothalamic in origin. Except when very strong stimuli were used, which spread to the hypothalamus, similar reactions could not be elicited from surrounding parts of the brain such as the thalamus, internal capsules, septum, and infundibular stalk." Ranson asserts further that "the hypothalamus is the centre for the integration of the visceral and somatic components of emotional expression. When it is removed, a fully developed emotional response is no longer possible and when it is stimulated electrically it can be made to call forth a typical rage reaction."

Hypothalamic stimulation of the *intact* animal elicits retraction of the ears, growling, raising of the back and lashing of the tail and the development of hyperpnea, salivation, mydriasis, piloerection, biting, striking movements with claws unsheathed, and finally precipitate running (Massermann). These reactions have been shown by Massermann to be poorly directed, diffuse, and stereotyped, and to last only as long as the stimulus is applied. Stimulation of the left mammillary body in lightly narcotized cats likewise has produced typical sham rage[8].

Support of these observations has been found in clinical experience. Irritation or stimulation of the hypothalamus by removal of tumors in this region has resulted in outbursts of uncontrollable emotional responses. Manic-like excitements with euphoria, motor restlessness, excitement, push of speech, and flight of ideas have been observed by Foerster[9] in operations on suprasellar tumors during the removal of which the hypothalamus was stimulated. Similar reactions have been observed by Fulton and Bailey[10]. In a 13 year old child operated on for glioma of the optic chiasm invading the third ventricle Cushing[11] found that he could produce tremendous hyperactivity and blind excitement by stimulation of the hypothalamus. Fits of meaningless and uncontrollable laughter have been recorded[12] in a patient with a tumor restricted to the region of the mammillary bodies, and loss of inhibitory control over the emotions has been found in an elderly male suffering from an adenomatous cyst. This patient made advances and ribald remarks to the nurses, all of which ceased after removal of the tumor.

There have been a few instances in which not only emotional excitement but personality deviations occurred. I do not wish to imply that here in the hypothalamus lies the master personality switch, but in the instances to be cited there occurred a combination of emotional and personality deviations for which there was no other cause found.

A case of personality disorder has been reported in a man of 39, who at necropsy was found to have a teratoma of the third

6. Kessler, M. M.: Spontaneous and Reflex Emotional Responses Differentiated by Lesions in Diencephalon, Proc. Soc. Exper. Biol. & Med. 47:225-227 (June) 1941.
7. Ranson, S. W.: Some Functions of the Hypothalamus, Harvey Lecture, Bull. New York Acad. Med. 13:241-271 (May) 1937.
8. Gellhorn, E.; Cortell, R.; Feldman, J.: The Autonomic Basis of Emotion, Science 92:288-289 (Sept. 27) 1940.
9. Foerster, O. and Gagel, O.: A Case of Ependymal Cyst of the Third Ventricle (A Contribution to the Question of the Relation of Mental Disturbances to the Brain Stem), Ztschr. f. d. ges. Neurol. u. Psychiat. 149:312-344, 1933.
10. Fulton, J. F. and Bailey, P.: Tumors in the Region of the Third Ventricle, J. Nerv. & Ment. Dis. 69:1-25 (Jan.); 145-164 (Feb.); and 261-277 (March) 1929.
11. Cushing, H.: The Pituitary Body and Hypothalamus, Springfield, Ill., C. C. Thomas, 1929.
12. Dott, Norman M.: In the Hypothalamus, London, Oliver and Boyd, 1938, p. 212.

ventricle destroying the hypothalamus[13]. About a year before signs of tumor developed he became irritable, hypersensitive, aggressive, argumentative, curt, stubborn, and unreasonable, all in contrast to his normal personality make-up. He had periods of great excitement and frequently flew into a rage over trivial matters. At other times quiet periods alternated with periods of excitement. His business judgment became impaired, he became indifferent to and careless of his professional responsibilities, and he exhibited a severe memory loss. In other ways he showed evidence of a loss of normal control over himself. The change in mood, intellect, and personality structure was so striking that he was thought to have general paresis. The teratoma found at autopsy extended from the region of the anterior commissure to the middle position of the mesencephalon. The thalamus, particularly the anterior and medial groups of nuclei, was compressed but not destroyed. In the hypothalamus the substantia grisea was completely destroyed; the nucleus supraopticus was severely damaged; the nuclei paraventricularis, and tuberis lateralis were destroyed completely. The nucleus tubero-mamillaris was quite well preserved bilaterally. The cerebral cortex showed no changes.

Here then was a patient with severe mood swings, intellectual deficits and personality changes, with widespread destruction of the hypothalamic nuclei without signs of hydrochephalus and with no evidence of cortical damage. A case very much like this was recorded by Dott in a man of 42 who had a large epidermoid cyst extending up into the hypothalamus but who had no increased intracranial pressure. Dott's patient showed personality changes characterized by acts of indecency; he showed also marked emotional lability, his mood swinging between euphoric complacency and mild depression, and at times venting itself in bouts of weeping or laughing. He too had disturbance of intellectual functions as evidenced by impairment of memory retention and some defect of judgment.

Further evidence for the occurrence of personality changes and disorders of the intellect in hypothalamic tumors is found in a few cases reported by Cox[14]. In one patient, a young man of 27, there was noted an inability to concentrate, carelessness, indifference to his shortcomings, coarseness of habits, and severe memory defects. He was found at operation to have a cyst in the pituitary region which had indented the hypothalamus. Removal of the cyst, which was a craniopharyngioma, resulted in a return to almost normal mentality three weeks after operation. The other case recorded by Cox concerned a woman of 65 who developed dullness and listlessness, trance-like states, gross memory defects, and disorientation. She was found at operation to have an adenoma which indented the hypothalamic region. Operation was followed by a return of memory and a reversal to a perfectly normal mentality after five weeks.

From all this evidence the inference appears justified that in both animals and man the hypothalamus is concerned with the motor expression of the emotions, chiefly emotional excitement. Further consideration will be given to the problem later, but it appears pertinent to our discussion at this point to introduce evidence which seems to demonstrate that it is not the hypothalamus alone which is responsible for the somatic aspects of emotional expression. Keller[15] has observed that typical sham rage can be elicited in animals in which only the cord, medulla, pons, and small caudolateral portions of the midbrain remain intact. Massermann[16] has produced evidence in support of this contention. In cats which have survived large bilateral lesions of the hypothalamus, electrical stimulation of juxtahypothalamic areas in the subthalamus or mesencephalon produces typical hypothalamic responses. "To be sure, these responses are not as well coordinated and are more easily exhausted than those in animals with an intact diencephalon, indicating that the hypothalamus probably functions in facilitating, integrating and perhaps reinforcing the bodily expressions of emotion. Nevertheless, the observations as a whole indicate that, with appropriate stimuli, not only emotional reactions but even their somatic accompaniments can occur despite the presence of extensive destruction of the hypothalamus and the primary neurones of its descending pathways."

13. Alpers, B. J.: Relation of the Hypothalamus to Disorders of Personality, Arch. Neurol. & Psychiat. 38:291-303 (Aug.) 1937.
14. Cox, L. B.: Tumors of the Base of the Brain; Their Relation to Pathological Sleep and Other Changes in the Conscious State, M. J. Australia. 1:742-752 (May 15) 1937.
15. Keller, A. D.: Autonomic Discharges Elicited by Physiological Stimuli in Midbrain Preparations, Am. J. Physiol. 100:576-586 (May) 1932.
16. Massermann, J. H.: Destruction of Hypothalamus in Cats, Arch. Neurol. & Psychiat. 39:1250-1271 (June) 1938.

2. *The Role of the Cerebrum.* That disturbances of emotional expression can occur as a result of cerebral lesions appears to be clear. I have mentioned the fact that rage expressions are more easily elicited in decorticate cats and dogs, probably because the hypothalamus is completely released from cortical control. Attention has been directed recently to the role of the hippocampal cortex in emotional reactions. Papez has shown that in lower vertebrates the medial wall of the brain is connected with the hypothalamus and that this connection is further elaborated in the mammalian brain by the development of the hippocampal formation. According to Papez[17], emotional stimuli pass first to the hippocampal formation and then by way of the fornix to the mammillary body. Thence they pass through the mammillo-thalamic tract to the anterior nuclei of the thalamus and then by the medial thalamocortical radiation to the gyrus cinguli. "The central emotive process of cortical origin may then be conceived as being built up in the hippocampal formation and as being transferred to the mammillary body and then through the anterior thalamic nuclei to the cortex of the gyrus cinguli. The cortex of the cingular gyrus may be looked on as the receptive organ for the experiencing of emotion as the result of impulses coming first from the hypothalamic region, in the same way as the area striata is considered the receptive cortex for photic excitations coming from the retina. Radiation of the emotive process from the gyrus cinguli to other regions in the cerebral cortex would add emotional coloring to psychic processes occurring elsewhere. This circuit would explain how emotion may arise in two ways: as a result of psychic activity and as a consequence of hypothalamic activity." These observations have been carried further by Kluever and Bucy in monkeys[18]. Bilateral temporal lobectomy results in definite changes described as psychic blindness, a tendency to examine all objects by mouth, an excessive tendency to take notice of and react to every visual stimulus—referred to as "hypermetamorphosis"—emotional changes, and an increase of sexual activity. The emotional changes are characterized by "either profound changes in emotional behavior or complete absence of all emotional reactions in the sense that the motor and vocal reactions generally associated with anger and fear are not exhibited." Specifically, the reaction of the lobectomized monkey consists of a loss of the wildness and the escape reactions of the normal animal, these being replaced by what is apparently an indifference and an absence of escape patterns. None of the reactions described appeared after unilateral lobectomy, after bilateral removal of the first temporal convolution, after unilateral or bilateral removal of the second and third temporal convolutions, or after severing the connections between temporal and frontal or temporal and occipital lobes. The findings of Kluever and Bucy seem to support the concept of Papez concerning the importance of the hippocampal area, since the emotional changes described occurred in an animal from which the hippocampus was removed, while in those in which the hippocampus was intact, none of the typical symptoms appeared.

Further experiments by Spiegel, Miller and Oppenheimer[19] in cats and dogs show that rage reactions appear with lesions of the olfactory tubercles, of the amygdaloid nuclei, and to some extent also with lesions of the hippocampus-fornix system. All of these areas are in close connection with the hippocampal system. No rage reactions were elicited with lesions confined to the frontal poles.

Finally, mention must be made of the observations of Fulton and Ingraham[20], who studied four cats with survival periods of one to three months after incisions were made in the brain anterior to the chiasm from the midline to the olfactory radiation. The experiments were undertaken on the supposition that the frontal lobes give rise to fibers which pass to the hypothalamus. Three cats showed marked rage reactions after a bilateral incision. A fourth cat showed no such response. Fulton and Ingraham concluded that their bilateral lesions had divided cortico-hypothalamic tracts. Unfortunately there is no good evidence that such tracts exist; at least they have not been demonstrated anatomically[21]. It is possible that impulses may reach the hypothalamus

17. Papez, J. W.: A Proposed Mechanism of Emotion, Arch. Neurol. & Psychiat. 38:725-743 (Oct.) 1937.
18. Kluever, H. and Bucy, P. C.: Preliminary Analysis of Functions of the Temporal Lobes in Monkeys, Arch. Neurol. & Psychiat 42:979-1000 (Dec.) 1939.
19. Spiegel, E. A.; Miller, H. R.; and Oppenheimer, M. J.: Forebrain and Rage Reactions, J. Neurophysiol 3:538-548 (Nov.) 1940.
20. Fulton, J. F. and Ingraham, F. D.: Emotional Disturbances Following Experimental Lesions of the Base of the Brain (Pre-chiasmal), J. Physiol 67:27, 1929.
21. Clark, W. E. Le Gros: The Hypothalamus, Edinburgh and London, Oliver and Boy, 1938, pp. 1-69.

from the frontal cortex by way of the septal and subthalamic region. Fibers from the septal region in the guinea pig have been described by Wallenberg as extending from the frontal pole to the antero-dorsal part of the septum. Corticofugal fibers have been traced also from the frontal pole to the zona incerta, whence fiber connections are made with the hypothalamus[21].

Emotional changes are found, then, in animals with cortical ablations of one form or another, chiefly with temporal lobe ablations, but likewise with interruption of frontal pathways. Support for these findings in human material has not been forthcoming in any degree, largely because of the difficulty of finding lesions confined to restricted cortical areas and because of the multiplicity of function attributed to focal regions of the cortex.

Additional indication of the occurrence of abnormal emotional reactions with lesions of other parts of the nervous system than the hypothalamus is given by cases of compulsive laughing and crying. Such cases reveal clinical features similar in some respects to those of uninhibited rage reactions seen with hypothalamic damage. The emotional expressions of laughing and crying are completely uncontrollable, are evoked by seemingly neutral and insignificant stimuli, and persist for only a short time after the stimulus is active. In all these features compulsive or pathological laughing and crying in the human being resemble the emotional responses seen in animals with hypothalamic lesions. Yet they may be evoked by damage in many parts of the nervous system. They may develop with lesions of the cortex, of the cortex and diencephalon, of the diencephalon alone, or of the midbrain and medulla. Recent studies of Davison and Kelman[22] indicate that destruction of frontal, motor, premotor, or sensory areas may be associated with pathological laughing and crying, and that these areas are connected with the hypothalamus. However many of the reported cases of pathological laughing and crying have been found in association with vascular disease, multiple sclerosis, or other scattered lesions, so that the possibility always exists that the gross softenings found may not indicate the full extent of the lesion responsible for the reaction.

22. Davison, C. and Kelman, H.: Pathologic Laughing and Crying, Arch. Neurol. & Psychiat 42:595-643 (Oct.) 1939.

A survey of cases of corpus callosum disease in man brings forth some additional data which may be pertinent. In cases of corpus callosum tumor one may sometimes observe a flatness in emotional responses characterized by apathy and indifference and somnolence which are often striking. Reactions of this sort have been found in patients with tumors confined to the corpus callosum—usually to its anterior portion—, and the type of reaction approaches the apathy described by others associated with lesions of the hypothalamus. In Marchiafava's disease, a primary degeneration of the corpus callosum, King[23] reports "emotional disorders, including states of exaggerated excitability and irascibility, leading to acts of violence." Since no cortical disease is found in such cases, the recorded emotional reactions assume some significance; however, the disease always occurs in alcoholic addicts and the symptoms cannot be taken therefore at their face value.

3. *The Role of the Nervous System.* In the assessment of the evidence at hand it is advisable once more to state that it is the physical expression of the emotions, with their associated sympathetic responses, which is under consideration, and not the emotion itself. It appears probable that the hypothalamus is concerned with emotional expression, and that it can be regarded as an integrating area for such reactions. This confined and restricted area is probably played upon by impulses from the cerebral cortex, particularly from the temporal area, but probably also from other portions, and is inhibited by the action of the cortex under normal circumstances. Excitatory as well as inhibitory mechanisms from cortex to hypothalamus have been postulated. The exact mechanism of interaction of the cortex and hypothalamus is not definitely known and cannot yet be stated. As Papez has pointed out, the circuit involved in the expression of the emotions passes through the posterior hypothalamus and the mammillary bodies, and it seems probable that in the hypothalamic region the main discharge occurs. Some regard the hypothalamus as playing a role in the reinforcement and coordination of the neutral and hormonal mechansims concerned in emotional expression[24].

23. King, L. S. and Meehan, M. C.: Primary Degeneration of the Corpus Callosum (Marchiafava's Disease), Arch. Neurol. & Psychiat 36:547-568 (Sept.) 1936.

24. Massermann, J. H.: Is the Hypothalamus a Center of Emotion?, Psychom. Med. 3:3-25 (Jan.) 1941.

There is little proof that the emotional reactions evoked by hypothalamic stimulation and by disease or ablation of this area are associated with the affective features of the emotions themselves. Massermann[24], for example, has found that in animals there is probably no direct relationship between hypothalamic function and affective experience, since "(a) the reactions induced by stimulation of the hypothalamus do not, within limits, greatly modify spontaneous emotional behavior (b) animals with extensive hypothalamic lesions react to emotional stresses and can apparently experience genuine affective states (c) animals subjected to prolonged conditioning procedures . . . do not learn to respond to either the sensory or hypothalamic stimuli in ways analogous to their spontaneous or experimental adaptations to situations of adequate emotional significance."

Animal experimentation emphasizes particularly the pseudo-affective types of reaction, the sham aspects of rage, and the absence of affect. Because of the difficulty in determining the presence of true emotional experience in an animal, human data are more reliable. The reported instances are not numerous, but there are some data pointing to the fact that something which simulates the affective features of emotional experience may be encountered with hypothalamic lesions. Thus in the case of tumor mentioned above[13] a true depression existed in a person who had never previously suffered from such a disorder, although of course it is not possible to assert that this was not a reactive depression. Grinker and Serota[25] found that on strong electrical stimulation of the hypothalamus anxiety sometimes appeared, persisting with crying and expressions of fear. Prolonged sobbing occurred in one case. On the other hand, White[26] has stimulated the hypothalamus in 8 human patients under local anesthesia without obtaining emotional reactions. Foerster observed manic reactions on stimulation of the hypothalamus, but did not say whether they were accompanied by an affective emotional state. The compulsive laughing and crying of pseudo-bulbar cases is usually referred to as without affect, but there is doubt as to whether one can exhibit all the physical features of an emotion without experiencing some of the psychological aspects of the emotional experience itself. The data available support the contention that the emotional expression of hypothalamic damage or stimulation in human beings may be associated with some sort of affective response. This is not to say of course that the hypothalamus is responsible for the affective features of the emotions.

The Effect of Organic Disease on Intellectual and Emotional Functions. Organic or structural disease leaves its mark on intellectual as well as emotional functions. It is impossible to cover of course the extensive problem of the relation of intellectual functions to the cerebral cortex, but it may be desirable for the purposes of our argument to indicate some of the data which serve to demonstrate further the inseparability of structure and function. Ablations of the cortex in animals result in various deficiencies of function. The chimpanzee deprived of his prefrontal areas can no longer manipulate sticks as tools in such a way as to solve problems in reaching for food. He shows also a memory defect in the inability to recall after a few seconds' delay the cup under which a piece of food has been hidden. Similarly, monkeys reveal an incapacity to perform this test after parts of the frontal lobes are destroyed. In many cases of destructive lesions of the frontal lobes in human beings similar effects on memory retention have been noted. Removal of the frontal lobe in human beings results in a loss of inhibitory control, a loss of energy, and difficulty in initiation and synthesis of ideas. Interruption of association pathways in the frontal lobes of patients with agitated depressions, schizophrenia, and obsessional syndromes has resulted in a loss of agitation and the development of a placidity not present before the operation. Freeman[27] speaks of a bleaching of the affective component connected with the consciousness of the self. "Reduction of the affective component allows the personality to appear in purer form, divested of certain restraining features, but essentially unchanged in regard to energy and intelligence, the principal change being an alteration in the direction of interests from within outward." It is conceivable that the loss of depressions and agitations following shock treatments in psy-

25. Grinker, R. R. and Serota, H.: Studies on Corticohypothalamic Relations in Cats and Man, J. Neurophysiol. 1: 573-589 (Nov.) 1938.

26. White, J. C.: Autonomic Discharge from Stimulation of the Hypothalamus in Man, A. Research Nerv. and Ment. Dis. Proc., 1939, 20:854-863, 1940.

27. Freeman, W. and Watts, J. W. W.: The Frontal Lobes and Consciousness of the Self, Psychom. Med. 3:111-119 (April) 1941

choses results from physiological interruption of association pathways. In animals such as the rat habits usually mediated through the cortex in the intact animal can be acquired with equal facility in the absence of the cortex, and the same may be true to a lesser degree in higher animals and man.

The occurrence of structural disease parading as a psychogenic disorder has long been noted, and it is a clinical axiom that many organic conditions may be manifested primarily as neuroses. The occurrence of neurotic traits as an early feature of general paresis, the lability of mood or the personality deviations in some cases of brain tumor, the diffuse somatic complaints of patients with pancreatic carcinoma are all sufficiently common to indicate the close relationship of structural and psychogenic mechanisms. This relationship is seen even more clearly in states of delirium due to organic factors of many sorts. A bodily disease explodes as a mental disorder, due in some instances to disturbances in brain metabolism, and in others to the absorption of chemicals and their direct effects on cell action. The changes in the mammillary bodies and the paraventricular nuclei in Korsakoff's psychosis are a further pertinent example. The problem is more clearly etched in the effect of hypoglycemia on brain activity. Nervous symptoms of many sorts develop, among them nervousness, tremor, drowsiness, anxiety, hysterical pictures, and many purely organic symptoms. Mild depression, difficulty in concentration, excitement, compulsions, fugues, hallucinatory states and many other psychogenic symptoms may appear. These are associated with changes in the brain cells and may be caused by the structural cell changes. Physiologically, as Himwich and his workers have shown, insulin hypoglycemia suppresses first the activity of the cerebral cortex, releasing subcortical mechanisms in the basal ganglia and hypothalamus. Later these mechanisms are suppressed and midbrain and medullary activity develops. This is a clear example of a structural disorder manifested by numerous so-called neurotic symptoms.

The result of decreased oxidation in the nervous system is illustrated further by the symptoms of oxygen lack. It has been suggested that anoxia acts by interfering with dextrose metabolism. The reaction of the nervous system to anoxia is well illustrated by the effects produced by high altitudes. Tremors, ataxia, and involuntary muscle movements are observed. Significant memory loss is observed also in subjects exposed to low oxygen tension. Average college students can remember eight or nine out of ten paired words, but the number is decreased if students are under low oxygen tension. Wortis[28] has suggested that the memory loss of age may be due to anoxia, and Cameron[29] has shown that there is a decreased oxygen consumption by the brain tissue in senile psychoses. Disturbances in affective behavior have been noted in normal subjects under conditions of low oxygen tension, manifested by impairment of emotional control, elation, flightiness, and mental dullness. Neurotics under similar conditions revealed an even greater lack of emotional restraint.

Lack of vitamins has been found recently to produce neurotic or psychogenic symptoms. Thiamin-poor diets have been found to produce fatigue, lassitude, anorexia, precordial pain, dyspnea, muscle cramps, and palpitation, all of which disappeared on the administration of thiamin. Similar symptoms have been observed in B complex deficiency. The Wernicke syndrome, characterized by mental confusion, ophthalmoplegias, and neuritis, has been produced in experimental animals by a diet deficient in thiamin, and the condition in human patients greatly relieved by the administration of thiamin. The mental confusion in these cases has been found to be due to a multiple vitamin deficiency. Cases of pellagra are sometimes associated with psychoses, due apparently to a combined thiamin and nicotinic acid deficiency. Of even greater significance, however, is the occurrence of what has been ineptly termed the neurasthenic syndrome in pellagra, characterized by fatigue, insomnia, anorexia, vertigo, nervousness, and anxiety, and relieved by nicotinic acid. Studies have shown that deprivation of the B complex results in impairment of judgment without evidence of impairment of other intellectual functions.

Summary

The data which I have presented presuppose a purely mechanistic approach to the problem of mental function and assume that a brain defect is followed by specific difficul-

28. Wortis, H.: Some Nutritional Aspects of Brain Metabolism, Psychiatric Quart. 15:693-714 (Oct.) 1941.
29. Cameron, D. E., Himwich, H. E., Rosen, S. R., and Fazekas, J. F.: Oxygen Consumption in the Psychoses of the Senium, Am. J. Psychiat. 97:566-572 (Nov.) 1940.

ties in function. This approach has been termed by Putnam the "mosaic" theory of cerebral function, opposed to which is the formulation that "cortical cells are to a certain extent equipotential, so that a reduction of brain mass has as one, at least, of its effects the diminution of the total available number of possible connections between various areas."[30] Goldstein, the proponent of the equipotential concept, has shown that after local brain damage there is impairment of many functions, affecting first the more complicated ones[31]. He states that "if by the mosaic theory is meant that any part of the cortex has a functional relation to a definite, separate performance, then I would say that the theory is wrong. If we mean by the mosaic theory that every part of the cortex *contributes* something different to the performances which in themselves are related to the *functioning of the whole cortex*, even the whole organism, then it is correct. There are no isolated performances which are merely expressions of the functioning of single parts of the organism, especially not of a separate part of the brain cortex. Any performance is a reaction of the total organism to some condition in the outer world."

How far is one justified in using biological data to explain psychological phenomena? In spite of valiant efforts to correlate the structural and the psychogenic, there still remains a wide gap which it seems almost impossible to span in our present state of knowledge. Although it is possible to say a good deal about the mechanisms which release the physical expression of the emotions, there is still little which can be said about the relation of structure to the experiencing of emotion. It may be that the answer will never be found in the pursuit of cell function, but it can hardly be denied that a broader knowledge of structure and function must lead inevitably to a more profound understanding of the workings of the human mind and body. In this sense, therefore, the broader use of physical mechanisms in psychiatry is to be encouraged, for it becomes more and more apparent that while structure and psychological function are not the same, they are nevertheless so interdependent that an understanding of the one is essential to a comprehension of the other.

30. Putnam, Tracy J.: The Significance of the Alterations of Mental and Emotional Processes Produced by Diseases of the Brain, A. Research Nerv. and Ment. Dis., Proc. (1938) 19:81-107, 1939.

31. Goldstein, Kurt: The Hypothalamus, A. Research Nerv. & Ment. Dis., 19:98, 1939.

UNDULANT FEVER FROM THE STANDPOINT OF THE GENERAL PRACTITIONER OF MEDICINE

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Malta fever, Mediterranean fever, or slow hospital fever was identified as a clinical entity as early as 1859. At that time clinical reports of this disease were confined to the island of Malta and the adjacent Mediterranean countries. Since that time the disease has been found in all countries of the world, and for that reason the designation which indicated that the disease is prevalent mainly in the Mediterranean region has been discontinued. The genus Brucella was named for Bruce in 1887[1], who isolated the first of this group of organisms which was called Micrococcus melitensis. The term Brucella has been accepted for the group of bacteria responsible for the disease in human beings and animals. The term brucellosis indicates infections produced by the Brucella group of bacteria.

The organism associated with contagious abortion of cattle was first isolated by Bang, assisted by Stribolt, in 1897[1]. At that time the organism was isolated from fetuses and fetal membranes of cows that had aborted and it was designated as the Bacillus abortus of Bang. The fact that the udder of the cow was the reservoir for Brucella abortus was announced by Schroeder and Cotton in 1911 and by Smith and Fabyan in 1912[1]. The chief host of Brucella melitensis was found to be the goat. This discovery was made in 1905 by Zammit, who found that agglutinins were present in the blood of goats on the island of Malta at the time the Mediterranean Fever Commission started its work[1]. It was found that the organisms could be isolated from the blood, udder, spleen and lymph nodes of the goat. Brucella suis was first isolated by Truam in 1914 from fetuses expelled prematurely by sows. Since that time Br. suis has become a well known member of this group[1].

Prior to 1918 not a great deal of interest

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1. Huddleson, I. Forest.: Brucellosis in Man and Animals New York, The Commonwealth Fund, 1939.

was given to Brucella infections in human beings. In 1918, Alice Evans demonstrated that the organisms of Malta fever (M. melitensis) and the organisms of contagious abortion of cattle (B. abortus) were closely related, and for practical purposes were indistinguishable[1]. These observations were of great importance and led to the discovery of the widespread occurrence of Brucella infections in both human beings and animals. The work of Huddleson and his associates is of major importance because of his contributions to bacteriological methods which led to the identification of various strains of Brucella organisms, his interest in developing a method of skin testing of human beings, and his continued efforts to develop a satisfactory therapeutic agent with which to combat this group of organisms. The veterinary profession has made important contributions relative to the pathological aspects and the distribution and prevalence of these infections in animals, and has developed practical administrative and technical procedures which have been shown to be valuable in the control of Bang's disease.

Brucella infection in human beings may be seen occasionally as a result of contact with dogs. While animals represent the main reservoirs of infection there have been occasional reports of brucellosis in fowls.

The incidence of Bang's disease in cattle in the United States in 1935 was found to be about 11.5 per cent[2]. In 1941 the incidence of positive reactors was 2.4 per cent. In that year Bang's disease was reported from every state in this country. From the point of view of the dairy industry, brucellosis constitutes a major financial problem. The milk production of infected herds may be reduced as much as 25 per cent, and the number of calves in a herd affected with Bang's disease may be reduced as much as 40 per cent. This infection has been demonstrated not only in dairy herds, but also in range cattle where lot feeding is practiced during the winter months.

Since the practical eradication of bovine tuberculosis has been accomplished in this country, Bang's disease is probably the most serious disease affecting cattle. It has been stated that from 38 to 50 per cent of all herds that have been tested in the United States showed the presence of reactors. The widespread dissemination of this infection among dairy cattle, and among range cattle in some areas, not only constitutes a major economic and veterinary problem, but also involves the possibility of reduced meat and milk production for human consumption. There is also the problem of transmission of the disease to the general population, especially to those intimately exposed to cattle.

The prevalence of this disease in hogs has not been studied sufficiently for any dependable statement to be made. It has been estimated that the incidence of infection, based on agglutination tests, is from 1 to 3 per cent. A study should be made to determine whether or not the disease is sufficiently prevalent in hogs to justify eradication measures. In certain areas in the United States Br. suis is more prevalent in human beings than is any other Brucella infection. This is especially true of the important hog raising area—namely, Iowa and adjacent states. The problem of infection with Br. melitensis, the caprine or goat strain of Brucella, in the United States is limited to those areas where goat raising is conducted on a commercial scale. Of the total amount of milk consumed in the United States, goat's milk represents a very small proportion. The chief goat raising areas in this country are found in the southwestern states, and it is from these areas that most of the cases of brucellosis of caprine origin have been reported.

Brucellosis in Man: Bacteriology

There are three species of the genus Brucella which are commonly associated with infection and clinical manifestation in human beings. In the order of their virulence, they are as follows:

Br. melitensis is associated with the most severe clinical manifestations, although everyone infected with this variety of Brucella does not necessarily manifest clinical symptoms. When Br. melitensis is associated with clinical symptoms the disease is likely to be severe. Since goat raising is not an important industry in the United States, we do not find many cases of Br. melitensis infection, although it is possible for imported dairy products to contain the organisms and cause an occasional case or group of cases in individuals.

Br. suis produces clinical manifestations

2. United States Department of Agriculture. Miscellaneous Publication No. 384. Benefits of Eradicating Bang's Disease.

which are next in severity to those caused by Br. melitensis. While no reliable data are available as to the prevalence of this infection in hogs, Br. suis in human beings is not uncommon. The majority of clinical Brucella infections in Iowa are reported to be of the suis variety.

Br. abortus represents the third strain found commonly in the United States. This organism is considered to be less virulent for human beings than either of the other two.

There is evidence that cross infections occur from the three varieties of Brucella organisms. On the whole goats do not become infected with the other two strains, but Huddleson[1] states that the infection of cattle with the goat strain has been found occasionally. Infection of swine with the abortus variety is rare, but infection of cattle with Br. suis does occur with relative ease, and epidemics resulting from Br. suis transmitted through cow's milk have been reported[3].

Prevalence

Since 1924 there has been an increasing number of cases reported each year. In 1938, there were 4,379 cases reported[4]. The number of reported cases, however, does not reveal the extent of this infection in the general population, as the infection may be present without the production of clinical manifestations.

The prevalence of Br. abortus infection in the general population is not known. Huddleson found that in a group of 500 individuals in Michigan composed of an equal number of males and females in all age groups constantly exposed to the abortus organism through an infected milk supply only 1.4 per cent showed evidence of infection and only 0.8 per cent showed any evidence of active infection.

Certain conditions in the general population may be associated with a relatively high prevalence of Brucella infection. In groups exposed to a milk supply containing Br. abortus, from 7.7 to 41 per cent were found to have Brucella agglutinins in the serum[5]. In our experience, 13.2 per cent of one group of individuals were found to have evidence of infection as indicated by the skin test.

In view of the lack of evidence of clinical activity, it is assumed that Br. abortus is an organism of relatively low virulence or that the susceptibility of man to Br. abortus is not very great. Another factor which may be operating to reduce clinical manifestations in human beings is the fact that milk is pooled and the dose of the organism is reduced. For this reason clinical infections resulting from Br. abortus are likely to be latent, asymptomatic infections or associated with mild or moderately severe manifestations.

Other groups in the population that may acquire Brucella infection are those in rural areas whose occupations bring them into direct contact with cattle and hogs. Workers on farms and veterinarians show a high incidence of infection. Those exposed to Brucella infection in laboratory work usually show a high percentage of infection.

Studies based on 991 cases in Iowa reported by Hardy and his associates[2] indicate that the annual average case rate is high in occupational groups exposed to animal sources of Brucella infection[6]. They found that among packing house employees the annual reported case rate per 100,000 was 142.5, among male workers on farms 14.5, and among females residing on farms 3.6. For other individuals in the population there was a rate of 3.0 per 100,000, and for children under 10 years of age the rate was 0.4. Similar data, based on skin tests, with reference to packing house employees have been reported by Meyer and by Heathman. These data indicate the importance of Brucella infection in certain occupational groups of the population and the necessity for specific control measures.

Additional epidemiological evidence is available to support the belief that these infections are more prevalent among certain groups. This is particularly true when the age and sex distribution of reported cases are analyzed; at least 75 per cent of the cases occur in males whose occupations bring them in direct contact with infected materials. More acute cases occur in males than in females, the acute cases probably arising as a result of direct contact during

3. Beattie, C. P. and Rice, R. M.: Undulant Fever Due to Brucella of the Porcine Type—Brucella Suis, J. A. M. A. 102:1670-1674 (May 19) 1934.
4. United States Public Health Service. The Prevalence of Undulant Fever (Brucellosis) in the United States. Pub. Health Rep. 53:1195-1216 (July 15) 1938.
5. (a) Stone, R. V. and Bogen, Emil: Studies of Correlated Human and Bovine Brucelliasis, Am. J. Pub. Health 25:580-588 (May) 1935.
   (b) Dooley, Parker: Undulant Fever: An Epidemic of Subclinical Infection with Brucella. Arch. Int. Med. 50:373-379 (Sept) 1932.
6. Hardy, A. V., Jordan, C. F., Borts, I. H. and Hardy, Grace C.: Undulant Fever with Special Reference to a Study of Brucella Infection in Iowa. National Institute of Health Bulletin, No. 158, December, 1930.

occupational exposure[7]. The age distribution of reported cases shows that a majority of these infections occur between the ages of 20 and 45. Clinical brucellosis in children is not seen very often.

Modes of Transmission

Brucella infection is transmitted mainly in two ways. First, it may be acquired through the ingestion of unpasteurized milk or cream which contains Brucella organisms. This method of transmission probably accounts for the majority of infections with Br. abortus, since unpasteurized milk products are still used extensively in the general population.

The second method of transmission of Brucella infection is through the skin. It has been shown by Morales-Otero experimentally in human volunteers that infection occurs more readily through the abraded skin than through the digestive tract[8]. Organisms which had been isolated for some time when fed to human volunteers did not produce infection by ingestion, but the same organisms produced the disease when placed on an abraded skin surface. Once the organisms penetrate the tissues of the body they enter the blood stream, remain there for varying periods of time and finally localize, probably in the reproductive organs, bones, spleen and lymph nodes of the body. In these tissues foci of infection are established from which the organisms escape from time to time to produce exacerbations of clinical manifestations.

Clinical Manifestations

Brucella infection in the general population may cause acute or chronic cases or may be latent and asymptomatic. The latter type occurs most often. The only evidence of brucellosis may be a positive skin test or a positive agglutination reaction.

The appearance of clinical manifestations will depend on the infecting strain of Brucella, the dose of organisms, the degree of exposure, the resistance of the patient, and whether the infection is transmitted by ingestion or contact with the skin. Those individuals who are in direct contact with contaminated tissues, blood or secretions of infected animals are most likely to develop clinical manifestations.

The ingestion of milk containing Brucella organisms of low virulence does not result in a majority of instances in acute cases. Infections that do occur are more likely to be asymptomatic or to cause the chronic type of case. The low incidence of clinical Brucella infection in children, who consume more milk than any other group in the population, may be explained in this manner.

The clinical symptoms of brucellosis are so variable that it is difficult for the physician to make a diagnosis of the disease without the aid of the laboratory.

The length of time between exposure and the onset of symptoms in naturally acquired infections may vary from seven to forty days. In experimental infections in human beings the incubation periods are reported to vary from ten to sixteen days. In an accidental infection in a packing house worker the incubation period was eighteen days.

The physician may encounter Brucella infection in four forms: (a) acute, (b) chronic, (c) subclinical, or (d) latent asymptomatic. The chief symptoms which characterize the acute forms of the disease are weakness, profuse sweating, fever, chilly sensations or chills, headache, pain in the joints and muscles, loss in weight, constipation, insomnia, cough and nervousness. On physical examination the findings are usually very few in comparison with the complaints of the patient. There may be evidence of weight loss, anemia and an enlarged spleen. Acute orchitis may occasionally be the first sign of the disease, and in some cases the onset of the disease may resemble influenza. The leukocyte count may be within normal range but there is usually a leukopenia with a relative lymphocytosis.

The chronic type of the disease is characterized by symptoms which in most instances do not resemble those seen in the acute forms of the disease. Many of the chronic cases follow acute attacks. The symptoms of chronic brucellosis are asthenia, emotional instability, nervousness, insomnia, loss in weight and generalized aching. In many instances a diagnosis of psychoneurosis or anxiety state is made in patients with chronic brucellosis.

The temperature in the chronic forms of the disease may or may not be elevated. When fever is present it is usually less than

7. (a) Heathman, Lucy S.: A Survey of Workers in Packing Plants for Evidence of Brucella Infection. J. Infect. Dis. 55:243-265 (Nov.-Dec.) 1934.
   (b) Meyer, K. F. The Heterogenous Infection Chains as Occupational Diseases. Arch. f. Gewerbepath. u. Gewerbehyg. 5:501-582, 1934.
8. Morales-Otero, P.: Further Attempts at Experimental Infection of Man With a Bovine Strain of Brucella Abortus, J. Infect. Dis. 52:54-59 (Jan.-Feb.) 1933.

101-102 F.; it may be present for varying periods of time, and usually recurs. The objective findings in chronic brucellosis are not very prominent.

The sub-clinical forms of brucellosis are usually of short duration and may resemble upper respiratory infections lasting three to seven days, with fever and malaise, joint pain or headache. Only one such episode of this nature may occur. Under such conditions the diagnosis may not be suspected.

In population groups exposed through raw milk or occupational exposure infection may occur without the development of clinical symptoms, or symptoms may be so mild that they escape detection. This latter group represents a large proportion of infected persons. It is this type of patient which may cause confusion in the interpretation of positive skin and agglutination tests.

The clinical course of Brucella infection may vary from an illness manifested by fever for a few weeks to a disease in which there are recurrences of fever and symptoms over a period of several years. The management of the patient in the early stage of the disease will determine to some extent the course of the disease in the future, so that early diagnosis is of paramount importance.

Diagnosis

The diagnosis of brucellosis in human beings is difficult because the organisms vary in virulence and there is a wide variation in clinical manifestations. The diagnosis can be made only after a careful history is obtained, a physical examination is made and certain laboratory procedures are performed. There are many other infectious diseases which may simulate undulant fever, and these must be excluded. The laboratory procedures which should be performed in making a diagnosis of undulant fever in human beings include a blood culture, which should be positive in a rather high percentage of acute cases and also in chronic cases which exhibit an exacerbation of symptoms. Occasionally, positive blood cultures may be obtained from individuals who do not at the time manifest any clinical symptoms. Techniques are available for cultivating the organism from the blood, but at the present time this is not practicable except in a few laboratories.

Since it is difficult to perform the one test which gives the best evidence of Brucella infection—namely, the blood culture—, the agglutination reaction and the skin test are the other procedures that can be carried out to obtain collateral evidence of Brucella infection. The agglutination reaction is positive in a high percentage of acute cases, although it may be negative occasionally. It may not be positive in the chronic case, and if it is positive it may be in a low titer, showing no decided rise in titer during the period of acute symptoms. This is in contrast to the agglutination reactions in acute cases. The agglutination test is negative in a high percentage of individuals who have asymptomatic infections. This was shown by studies made in institutional groups, where 4.8 per cent of individuals had positive skin tests while only 1.0 per cent of the same persons had a positive agglutination test. Huddleson and his associates have reported similar data for 855 individuals with positive skin tests, in whom only 13.1 per cent showed positive agglutination reaction by the rapid method[9]. Thus the agglutination reaction is not a reliable method to determine the prevalence of Brucella infection in population groups in which epidemiological studies are indicated. Occasionally a positive agglutination for Bacillus tularense may be seen in patients who have brucellosis.

The skin test can be performed with either a Brucella vaccine or the nucleoprotein suspensoid known as brucellergen, which was described by Hershey[10]. This is a reliable method to determine the presence of infection. The skin test is positive in about 95 per cent of individuals who have been infected with one of the three varieties of Brucella, and a positive reaction indicates a state of sensitivity or an allergic reaction. A positive skin test gives no evidence as to the clinical stage of the disease, and should not be used alone as a basis for making a diagnosis of clinical brucellosis. The skin test can be compared with the tuberculin test, in that it indicates a state of sensitization of the tissues and not necessarily an active infection. The skin test may remain positive for a long time in an infected person, and in our experience a majority of individuals found to have positive skin tests do not exhibit clinical manifestations.

The skin test is performed by injecting

9. Huddleson, I. Forest, Munger, Myrtle, Gould, S. E., and Paulson, Doris: A Study of Brucella Infection and Immunity in Humans. Am. J. Trop. Med. 17:863-880 (Nov.) 1937.

10. Hershey, A. D.: The Chemistry of Brucella. Thesis, Michigan State College, 1938. Unpublished.

0.1 cc. of brucellergen intracutaneously in the flexor surface of the forearm. It should be read forty-eight hours after injection. A positive reaction is characterized by a circumscribed area of erythema, edema and infiltration, which may vary in size from 10 to 70 mm. A reaction of 5 mm. is considered positive by some authors. There is rarely any necrosis or sloughing of the tissue at the site of local reaction. In infected persons who have symptoms the skin reaction may be accompanied by more marked manifestations of the symptoms present. Those who are very sensitive will show a systemic reaction along with the local manifestations and may develop lymphangitis above the site of injection. Frequently, erythema without edema or infiltration occurs within the first twenty-four hours. This type of reaction should be interpreted as non-specific. It usually fades within the next twenty-four hours.

When Brucella vaccine is to be used as a skin testing agent it should be diluted for such purposes with physiological saline solution so that there will be not more than 200,000,000 organisms per cubic centimeter[11]. The skin test dose should not be more than 0.1 cc. of diluted vaccine or approximately 20,000,000 organisms. In sensitized persons Brucella vaccine will produce abscess formation at the site of injection if the dose is too large. However, if the dose is small, abscesses will not often be seen and the reactions are comparable to those produced by the injection of brucellergen.

In the last few years Huddleson and his associates have been using a phagocytic test to determine the relative degree of resistance in individuals with Brucella infection. This test should not be considered a diagnostic procedure, but it can be used to determine the opsonic response of the patient to Brucella infection and it is one indication of an immunological response on the part of the patient to his infection. The resistance of a patient with Brucella infection may vary from time to time, and the opsonic index will be found to vary accordingly. Huddleson considers that in the case of Br. abortus and Br. suis infections this test is a good indicator of the patient's resistance to his infection. However, this procedure, while accepted by some investigators, has not been considered an accurate indication of the degree of resistance by others.

In making a diagnosis of Brucella infection the clinical manifestations exhibited by the patient should be considered together with the laboratory procedures available.

Control and Prevention in Man

The reservoir of infection with Brucella is primarily in animals, and the prevention of the disease in human beings depends upon the eradication of sources of infection in animals. The danger of Br. abortus infection from milk can be reduced almost to a minimum by adequate pasteurization of milk supplies. In rural areas where known infected animals supply milk to individual homes, the home pasteurization method could be applied to the family supply or the reactors could be removed. Thus by the use of pasteurized milk the great majority of the population could be protected from Brucella infection.

The pasteurization of milk, however, will not protect certain groups in the population whose occupation brings them into direct contact with infected animals. By a systematic educational program designed to inform these people of the danger of infection, and by advocating the use of prophylactic procedures it should be possible to reduce the number of infections even in these groups. Farmers and veterinarians should protect their hands and arms while attending cattle during parturition. It is well known that such groups do not make use of protective measures which are available. For workers in packing plants, protection of the exposed parts of the body should be effective in preventing infection with the Brucella group of organisms. Emphasis should be placed on the use of preventive measures by those groups in packing plants occupying the most hazardous positions.

A high percentage of individuals working in laboratories acquire Brucella infection either in clinical or subclinical form at some time by the handling of infected tissues or cultures of Brucella. The highly contagious nature of Brucella should be made known to laboratory workers. Such materials should be handled with the greatest care. Protection for the hands should be provided and the possible ingestion of cultures through pipettes avoided.

11. Keller, A. E.: A Comparison of Skin Reactions by the Use of Brucella Nucleoprotein (Brucellergen) and of Heated Brucella Organisms in Sensitized Individuals. South. Med. Jour. 33:1180-1184 (Nov.) 1940.

Treatment

It may be said that up to the present time no remedy of a chemical or biological nature has been proven to be a specific therapeutic agent in cases of brucellosis. Generally speaking a high proportion of patients in whom the diagnosis is made in the early weeks of the disease and who are given bed rest and symptomatic treatment respond favorably to almost any form of therapy. If six to eight months elapse before treatment is begun the response may not be satisfactory. Early diagnosis depends upon suspecting the disease and applying the proper laboratory tests. It is difficult to evaluate any form of treatment in a disease such as brucellosis, because a majority of patients will either recover permanently or obtain temporary relief from the disease without treatment.

Foshay has developed an anti-brucella goat serum which is reported to be effective in early cases. This agent, however, is not available through commercial channels. The same investigator has developed an oxidized detoxified vaccine which he uses in the treatment of chronic cases. Brucella vaccine containing suspensions of Br. suis and abortus killed by heat or formalin is used extensively. In the use of such an agent care should be exercised in the matter of dosage because of undesirable local reactions in patients who are sensitive to Brucella protein. Good results have been reported with vaccine.

In cases seen before the tenth week of illness Huddleson advocates the use of brucellin, which is a filtrate of a Brucella culture. The patient is given an intracutaneous test dose of 0.1 cc. to determine sensitivity. Following that brucellin is injected intramuscularly, the dose depending upon the degree of sensitivity of the patient. The material produces a marked systemic reaction and is nonspecific. The number of doses of brucellin necessary depends upon the stage of the disease and the reaction of the patient. Good results have been reported following treatment with this substance. It is not available commercially except from the Michigan State College at East Lansing.

Fever therapy either by the use of intravenous injections of typhoid vaccine or by means of the electric fever cabinet has also been used with good results. Such methods of treatment require hospital equipment and specially trained nursing personnel.

Since the advent of the sulfonamide drugs all forms of brucellosis have been treated with them. Sulfanilamide has been used in more cases than has sulfapyridine or sulfathiazole. Opinion is divided as to the efficacy of these drugs. In our experience they have produced good results in acute cases diagnosed in the early stages of the disease. In chronic cases poor results have been obtained. The number of chronic cases may be reduced by early diagnosis and treatment of acute cases before the organisms have established foci of infection in various areas of the body.

General supportive measures such as bed rest, maintenance of the fluid balance and nutrition of the patient, and the administration of iron to combat the anemia which is a common accompaniment of this disease are important procedures. Transfusion of whole blood or the administration of serum is a useful adjunct in the treatment of brucellosis. Blood or serum from immune donors has given good results.

The diagnosis of Brucella infection may be very difficult and should be made with caution, for the public looks upon undulant fever as a disease producing a protracted illness for which there is no specific remedy and a great deal of harm can be done to individuals in whom an incorrect interpretation of the clinical and laboratory data is made. Therefore, a complete review of all points in a case should be made and other infectious processes excluded before a diagnosis of brucellosis is made.

Donors' Curiosity. 50,000 blood donors may well ask 100,000 questions, which are succinctly answered by Fowler and Borer (J. A. M. A. 118:421 (Feb. 7) 1942). Donation of 555 cc. of blood causes an average drop of 2.3 Gm. hemoglobin (15% in Hawaiian male standard.) It takes about 50 days to replace this. Smaller losses regenerate earlier, and earlier in men than in women. Administration of iron shortens the regeneration time to 35 days.

Routine bleedings should be spaced at 3 months, unless controlled by hemoglobin estimations.—Clinico-Pathologic Comment, Hawaii Medical Journal 1:265 (March) 1942.

Tuberculosis in the Army. Medical tests of Canadian army recruits are being sharpened to the point where today only about one out of 1,000 men develop tuberculosis after being accepted in the army. Since May, 1941, a total of 895 men have been discharged from the army because of pulmonary tuberculosis, but of that number 251 had served for several months before being X-rayed. —Major G. T. Zumstein, Royal Canadian Army Med. Corps., Bulletin Tuber. Assn., March 1942.

SURGICAL DISEASES OF THE SPLEEN, WITH A REVIEW OF THE SPLENECTOMIES AT THE DUKE HOSPITAL DURING THE PAST TEN YEARS

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The first splenectomy, as far as is known, was performed by Fioravanti in 1549[1]. In the four centuries since then, not a great deal of progress has been made. In 1857, 83 cases were reported in the literature, and the diagnoses, when interpreted under our present diagnostic headings, were quite similar to conditions for which splenectomy is now performed. They included primarily wounds, abscesses, torsion, and blood dyscrasias. The use of splenectomy for blood dyscrasias was then, and still is a matter of debate. At one time or another splenectomy has been tried for practically every known type of blood disease. It is only by repeatedly charting, cataloguing and reviewing the results obtained, not only at operation, but also at definite follow-up intervals that we can evaluate the benefits to be expected and determine when surgery is indicated. It is with this aim that the following classification of surgical diseases of the spleen is presented, and the statistical results of splenectomy on 35 patients are analyzed and reported (fig. 1).

The following classification has been devised as being both complete and logical:

I. Surgical emergencies of the spleen
  A. Rupture
    1. Traumatic
    2. Spontaneous
  B. Torsion of the spleen

II. Infectious diseases
  A. Abscess of the spleen
  B. Splenitis
  C. Syphilis of the spleen
  D. Tuberculosis of the spleen
  E. Echinococcus cyst

III. Tumors of the spleen
  A. Primary or true cysts
    1. Congenital infoliation cysts
    2. Dilatation cysts
    3. True neoplasms or neoplastic cysts
      a. Lymphangioma
      b. Lymphangiosarcoma
      c. Hemangioma
      d. Endothelioma
      e. Fibroma
      f. Fibrosarcoma
      g. Dermoid
      h. Epidermoid
  B. Secondary or pseudocysts
    1. Traumatic
    2. Degenerative
    3. Parasitic

IV. Blood dyscrasias
  A. Those in which splenectomy is specific and curative
    1. Congenital hemolytic icterus
    2. Acquired hemolytic icterus
    3. Thrombocytopenic purpura
  B. Those in which splenectomy is of questionable value
    1. Sickle cell anemia
    2. Splenic anemia
    3. Banti's disease

Surgical Emergencies

There are two conditions in the spleen which may create a surgical emergency—rupture and torsion. Rupture constitutes by far the largest proportion of these. This may be either traumatic or "spontaneous".

A. *Rupture.*

1. *Traumatic rupture* of the spleen is seen not infrequently, and there is a characteristic history of injury, with subsequent pain and ensuing shock. The symptoms and signs are those of blood in the peritoneal cavity. The diagnosis is not difficult except in the so-called *delayed* or *subcapsular* rupture of the spleen. In this condition the splenic pulp and fibrous tissue are torn, but there is no division of the peritoneal surface until tension, due to hemorrhage, becomes great enough to rupture the capsule. This rupture may occur at any time from a few hours to five or six days, or even longer, after the original injury. Pain initiated by slight or severe trauma and referred to the left shoulder is almost pathognomonic.

2. *Spontaneous rupture* of the spleen is quite rare, and such a diagnosis should not be made until the history has been very carefully scrutinized. In the literature, however, one finds case reports which are almost irrefutable[2]. Some of these ruptures have occurred in spleens diseased with malaria

1. Phillips, J. R. and Knoepp, L. F.: Role of Splenectomy, Am. J. Surg 48:617 (June) 1940

2. Bologna, M: Spontaneous Rupture, Reforma Med. 56:869 (July) 1940.

DISEASE	*No. of Cases*	*Hospital Deaths*	*Late Deaths*	*Unimproved*	*Improved*	*Cured*	*Percent. of cures*	*Mortality*
Rupture	2					2	100%	
Congenital hemolytic jaundice	8					8	100%	
Acquired hemolytic jaundice	1					1	100%	
Thrombocytopenic purpura	2					2	100%	
Sickle cell anemia	5	1*		1	3			20%
Splenic anemia	5				5			
Banti's disease	9	3	3	1	2			33%
Painful splenitis	1					1	100%	
Indeterminate	2			2				
TOTALS	35	4	3	4	10	14		
Total Percentages		11.4%	8.6%	11.4%	28.6%	40%		

*Died of pneumonia

Fig. 1. Analysis of splenectomies performed at Duke Hospital during the past ten years.

or in myelogenous leukemia with splenomegaly[3]. A case of spontaneous rupture of a normal spleen during labor[4] and another during typhoid fever[5] have been reported. C. K. Chi, in 1939, gathered 13 well authenticated cases from the literature[6].

B. *Torsion.*

Torsion of the spleen is found most frequently as a complication of the so-called "wandering spleen". Occasionally the spleen has a long pedicle, so that it may migrate according to the patient's position. Some surgeons have advised a splenopexy for this condition, but the general feeling now is that either the spleen should be removed as an elective procedure[7], or the patient should be thoroughly acquainted with the situation and splenectomy performed only for definite symptoms of torsion[8].

Infectious Diseases

The spleen is considered resistant to infection because of its abundant blood supply. However, numerous cases of solitary metastatic abscess, with or without a perisplenitis, are reported. One typhoid abscess of the spleen has been reported[9]. Although the literature contains several reports of primary abscess of the spleen[10], it is difficult to exclude some initial focus of infection. It is quite possible for an acute abscess to develop into a chronic splenitis, and this sometimes happens. Splenectomy is indicated in both of these conditions. Drainage of an abscess, even when it is performed in two stages, carries a high mortality.

Involvement of the spleen is seen in both the secondary and tertiary stages of syphilis, and if swelling and pain do not disappear after several months of adequate therapy splenectomy is indicated.

Tuberculosis of the spleen is not unusual, and it is commonly associated with widespread disease elsewhere. If the spleen alone is involved splenectomy may be very beneficial to the patient, as death invariably results otherwise[11].

Echinococcus cyst is actually an infection, but it will be considered under cysts of the spleen.

Tumors of the Spleen

Almost all tumors of the spleen are of a cystic nature. Fowler has given a very thorough classification of cysts[12]. Goldberg recently collected numerous reports of solid splenic tumors from the literature and added 4 cases of his own[13]. The incidence of these

3. (a) Solar, P. Saurez: Rupture of a Malarial Enlarged Spleen Producing Internal Hemorrhage, Rev. Med. Quir de Oriente 1:11 (March) 1940.
   (b) Neal, J. M.: Rupture in Myelogenous Leukemia, M. Bull. Vet. Admin. 17:96 (July) 1940.
4. Shannon, W. F.: Spontaneous Rupture During Labor, Am. J. Obst. and Gynec. 40:323 (August) 1940
5. Roberson, Foy: Solitary Cysts of the Spleen, Ann. Surg. 111:848 (May) 1940.
6. Chi, C. K.: Spontaneous Rupture of Normal Spleen, Chinese M. J. 56:374 (Octber) 1939.
7. Romit, C.: Preoperative Diagnosis of Torsion of Pedicle of Spleen: Report of Case with Splenectomy Followed by Recovery, Arch. Surg. 41:781 (September) 1940.
8. (a) Bokrer, J. V. Torsion Wandering Spleen, Ann. Surg. 111:416 (March) 1940.
   (b) Peple, W. L.: Case of Spleen in Pelvis and Twisted on Pedicle, Virginia M. Monthly 67:208 (April) 1940.
9. Ransohoff, J. L. and Rourke, W. O.: Typhoid Abscess of Spleen in Hemolytic Jaundice, J. A. M. A. 114:2543 (June) 1940.
10. Brandt, L.: Primary Abscess of the Spleen of Unknown Origin, Ugesk f. Laeger 102:442 (May 2) 1940.
11. Pool, E. L., in Christopher: Textbook of Surgery, Philadelphia, W. B. Saunders.
12. Fowler, R. H.: Cysts of the Spleen, International Abstracts Surg. 70:213, 1940.
13. Goldberg, S. A.: Primary Neoplasms of Spleen, Am. J. Clin. Path. 10:700 (October) 1940.

solid tumors is low. At the Boston City Hospital, 2 such cases were found in 40,000 admissions and three hemangiomas were found in 1900 autopsies. Several epithelial and epidermoid cysts have been reported[14]. Several argentaffine tumors have been reported in the Japanese literature[15].

The majority of splenic cysts are large and contain old blood and a serous lining. There is considerable doubt concerning the etiology; degeneration and late results of trauma and hemorrhage are the most important probable causes[16, 5].

According to Fowler[12], true cysts account for 21 per cent of all cases and false cysts for 79 per cent. Of the true cysts, echinococcus ones are twice as common as all others. Cysts of the spleen are also said to occur in 2 per cent of all cases of hydatid disease. Seventy-one per cent of the false cysts are hemorrhagic. There is a history of malaria in 74 per cent of these cases, of syphilis in 11 per cent, and of trauma in 23 per cent.

Blood Dyscrasias

A. *Those in which splenectomy is specific and curative*

We find three types of blood disease in which splenectomy is indicated and, for all practical purposes, is curative. Two of these, congenital or familial hemolytic icterus and acquired hemolytic icterus, differ only in the antecedent history. The course of both types of the disease may be mild, although acute phases of jaundice and blood destruction are often initiated by infections such as tonsillitis and sinusitis. The diagnostic findings are the presence of micro-spherocytes, increased fragility of the cells, and active regeneration of the erythrocytes. The spleens are large (fig. 2A). Splenectomy produces an immediate remission of symptoms and a rapid rise in the hemoglobin. Three children from one family who suffered from the disease are shown in figure 2A. A 17 year old brother also had episodes of jaundice. All four had their spleens removed in April, 1939, and figure 2B shows the same three children sixteen months later. One can see a rather marked change in the general condition and growth

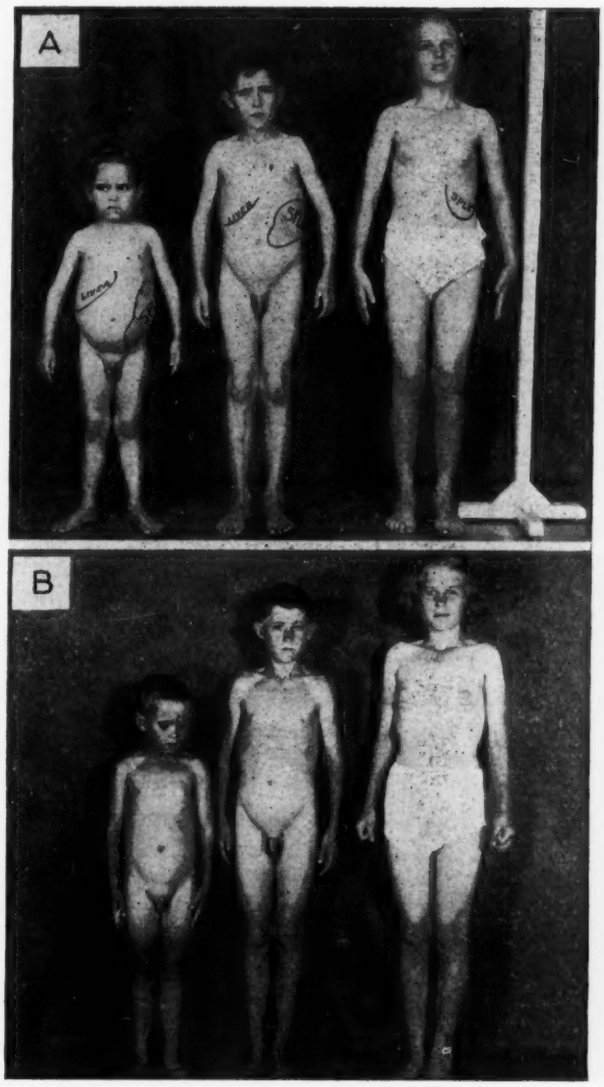

Fig. 2A. Three children from one family with hemolytic icterus before splenectomy.

Fig. 2B. The same children sixteen months after splenectomy.

of each child. Their hemoglobin determinations on the original admission were 23 per cent, 45 per cent, and 50 per cent. In 1940, they were 80 per cent, 88 per cent, and 83 per cent. Nine cases of hemolytic jaundice were studied (fig. 1), but the fragility tests were run preoperatively and postoperatively in only three. In two of these the fragility decreased somewhat but did not become normal, and in one it did not change. The cause of the increased fragility has been the subject of widespread study. C. Tsai, J. S. Lee, and C. H. Wu[17] have shown striking differences in the fragility of red cells taken from

14. (a) Kaijser, R.: Cystic Tumors of Spleen, Epithelial Origin, Upsala laekaref. foerh. 45:261, 1939.
(b) Lereboullet, P.; Gregoire, R.; Bernard, J.; and Ibarran, R.: Epidermoid Cysts of Spleen With Report of Case in Child, Sang. 13:853, 1939.

15. Nakano, T.: Argentaffin Tumors of the Human Spleen, Tr. Soc. Path. Jap. 30:68, 1940.

16 (a) Cyst of Spleen, Cabot Case 26252, New England J. Med. 222:1052 (June 20) 1940.
(b) Cole, F. L. and Forsee, J. H.: Cavernous Hemangioma of Spleen, Surg. 8:639 (October) 1940.

17. Tsai, C.; Lee, J. S. and Wu, C. H.: Role of Spleen in Altering Erythrocytic Fragility, Chinese J. Physiol. 15:165 (April 30) 1940.

the splenic artery and of those taken from the splenic vein. Their experimental studies show that changes in the Ph of the blood have a mild effect on cell fragility and that variations in the amount of time the blood has remained in one place have a marked consistent effect. They conclude that the greatest cause for the increased fragility is the stagnation of blood in the splenic sinuses. Among the deleterious effects of the disease are the formation of gallstones in 70 per cent of the adults (presumably due to the hyperbilirubinemia[18]), hyperplasia of the bone marrow, widening of the bones, and retardation of growth[19]. Langston[20] reported a case of infantilism associated with hemolytic icterus, which improved rapidly after splenectomy.

Hemorrhagic purpura which is definitely of the thrombocytopenic type can be cured by removal of the spleen unless the disease has been present long enough to cause excessive liver damage. Some authors have ascribed this diminution of platelets to platelet reducing substances in the spleen[21]. Not all are in agreement with this hypothesis, however. Wilensky[22] and others[23] have advised operation during a remission of the bleeding, but at times splenectomy may be compulsory during the acute stage as a life saving measure. The platelets rise sharply after operation, and several cases of thrombosis of the remaining portion of the splenic vein and of the portal system have been thought to be due to this rise. In general, a permanent cure is obtained. Most of the reported recurrent episodes of bleeding clear up when chronic infections are eliminated[24]. In one of my cases, the platelet count ranged from 0-12,000 during ten preoperative days and then rose to 780,000 forty-eight hours after operation. During the next few months, the count was estimated at from 400,000 to 550,000.

18. Pemberton, J. deJ.: Indications for Splenectomy, South. Med. and Surg. 102:46 (February) 1940.
19. Diamond, L. K.: Indications for Splenectomy in Childhood, Am. J. Surg. 39:400 (February) 1938.
20. Langston, W.: Hemolytic Icterus with Infantilism, South. M. J. 28:316 (April) 1935.
21. (a) Hodge, I. G. and Strong, P. T.: Effect of Splenic Extracts of Patients with Thrombocytopenic Purpura on Platelet Count of Rabbits, Bull. Ayer Clin. Lab. Pennsylvania Hospital 3:267 (December) 1939.
    (b) Pubegni, R.: Existence and Mode of Action of Thrombocytopenic Factor, Polioclenico 47:1 (January) 1940.
    (c) Hobson, F. C. G. and Witts, L. J.: Platelet Reducing Extracts, Brit. M. J. 1:50 (January 13) 1940
22. Wilensky, A. O.: The Indication for Splenectomy in the Association of Anemia and Splenomegaly, Surg. 9:99 (January) 1941.
23. Collins, H. O.: Indications for Splenectomy, South. M. J. 33:656 (June) 1940.
24. Pemberton, J. deJ.: The Diagnosis and Treatment of Purpura Hemorrhagica, Am. J. Surg. 24:793 (June) 1934.

Occasional recurrences have been ascribed to the hypertrophy and hyperplasia of remaining accessory splenic tissue. Wilensky[22], Settle[25], and others have emphasized the importance of searching carefully for any accessory spleens and removing them.

B. *Those in which splenectomy is of questionable value.*

There are three commonly encountered blood diseases in which splenectomy is justifiable, but frequently has little, if any, effect upon the course of the disease. These are: (1) sickle cell anemia, (2) splenic anemia, and (3) Banti's disease. In the group studied there were 5 cases of *sickle cell anemia* for which splenectomies were performed; three patients are improved, one is unimproved, and there was one death due to pneumonia. The patients who showed improvement have been followed from two and a half to six years, and have frequently had recurrent attacks of abdominal pain. The unimproved patient has continued to have leg ulcers.

This disease is, of course, confined to the Negro race. Sickle cells are formed within a few moments to twenty-four hours after the blood is drawn. This effect is lessened after splenectomy, but by no means arrested. It is hoped that splenectomy helps the patient by removing the organ in which stasis is most pronounced and destruction of erythrocytes is greatest.

Under the heading of *splenic anemia* are included the idiopathic hemolytic anemias with splenomegaly. Little has been added to Osler's description of this disease. Improvement may be expected to follow splenectomy if the syndrome has not been present long enough to cause secondary cirrhosis and ascites.

Banti's disease is an indefinite syndrome probably representing a terminal entity resulting from a number of related preceding conditions[22].

In both of these conditions splenectomy lightens the load thrown on the liver by reducing by at least 20 per cent the blood in the portal circulation; it removes possible toxic substances originating in the spleen; and it removes the splenic factor in the destruction of blood[24].

Omentopexy should probably be done in conjunction with splenectomy, as it assists the establishment of collateral circulation.

25. Settle, E. B.: Surgical Importance of Acessory Spleens, Am. J. Surg. 50.22 (October) 1940

Ligation of the coronary vein[26] has also been advised as an aid in preventing esophageal varices and hemorrhages. This procedure is apparently of little value, however, as the Mayo Clinic still reports postoperative gastric hemorrhages in 50 per cent of these cases[18]. Our series of splenectomies includes 5 cases of splenic anemia, with no mortality and with improvement in all. There are 9 cases of Banti's disease in this series. Three of these patients died in the hospital; three died within four to eighteen months; 1 is still having gastric or esophageal hemorrhages, and 2 are definitely improved.

Operative Considerations

The operative mortality is influenced by the original disease, the severity of anemia, the degree of hepatic damage, and the age of the patient. Glucose should be given preoperatively. Vitamin deficiencies and abnormalities of the protein content and of the albumin-globulin ratio, which are usually present, especially in the cases with ascites, should be corrected as far as possible. Wound disruption is frequent, and occurred in 3 of our cases. All of them were patients with Banti's disease and all had ascites. The operation is of little value and is probably contraindicated in such late cases.

Preparations for a transfusion should be made before the operation, in case this is necessary, and a basin containing citrate solution should be available. In case of the severe hemorrhage which occurs if the pedicle is accidentally torn blood may be siphoned or sponged into this basin and immediately reinjected into the patient[27]. This was done in one of my cases. An immediate auto-transfusion may be obtained by the injection of 1 cc. of adrenalin into the spleen one minute before clamping the splenic vein. The erythrocytes may be increased by as much as 800,000 to 1,000,000 cells, as has been demonstrated by Whipple.

Summary and Conclusions

1. The results of splenectomy on 35 patients are presented.
2. Infectious diseases are found to be very rare.
3. Tumors of the spleen are infrequent and are usually false cysts.
4. Although splenectomy has been performed for practically every known blood dyscrasia, it is of proven value in only three types:
   a. Familial hemolytic icterus
   b. Acquired hemolytic icterus
   c. Thrombocytopenic purpura
5. Only 2 out of 9 patients with Banti's disease improved; 3 died in the hospital, and 3 more died within two years.
6. Of the 35 patients on whom elective splenectomies were performed, 11 per cent died in the hospital, and there were 8.5 per cent late deaths; 11 per cent were considered unimproved, 28 per cent improved and 40 per cent cured.

26. Rowntree, L. G.; Walters, Waltman; and McIndoe, A. H.: A New Procedure in the Management of Cirrhosis of the Liver, Proc. Staff Meet., Mayo Clinic 4:121 (April) 1929.
27. Johnson, P.: Auto Transfusion in Rupture, West Virginia M. J. 36:127 (March) 1940.

THE ENDOCRINE FUNCTIONS IN PREGNANCY

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The maternal organism undergoes fundamental modifications during pregnancy. From the time of conception to the time of delivery there are manifold changes occurring, not only in the reproductive organs and mammary glands but also in the organism generally. These changes are influenced by the hormones elaborated during this period. The finely coordinated events occurring during pregnancy are made possible by an interplay of endocrine factors. The great advances of recent years in the field of female endocrinology have elucidated many of the bodily changes occurring during pregnancy and have led to the justifiable hope that a knowledge of abnormalities in the endocrine balance during pregnancy might throw light on the pathological states affecting reproduction, and might suggest appropriate therapeutic procedures[1].

All three of the female sex hormones—the estrogenic, the progestational and the gonadotropic hormones—play a role in normal pregnancy, as is evidenced by the high concentrations in which they appear and the changes in their titer during gestation. We shall, therefore, consider each of these hormones separately and attempt to assign to each its specific functions.

Presented before the Interurban Obstetrical and Gynecological Club, Winston-Salem, February 23, 1942.
From the Department of Internal Medicine, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem.

1. Grollman, A.: Essentials of Endocrinology, Philadelphia, J. B. Lippincott Co., 1941.

Estrogens

In the human female (this is not true of all other species) the estrogen content of the urine increases until parturition, after which it rapidly declines. The amounts excreted in different individuals vary from 15,000 to 80,000 international units per liter of urine in the first half of pregnancy. Practically all of this estrogen (97 to 98 per cent) is excreted in the form of the physiologically inert glycuronate, until just before the commencement of labor, when 10 to 20 per cent is excreted in the free form. However, the fact that this increased excretion of the free hormone does not consistently appear throws doubt on the assumption that it plays a part in inducing labor. As labor proceeds, the amount of estrogen excreted may diminish. In non-pregnant women the proportion of estrone to estriol is 1:1, but during pregnancy the ratio of these substances may vary from 1:1 to 2:3[2].

The Progestational Hormone

The corpus luteum plays an important role during pregnancy. Following ovulation, the hormone of the corpus luteum effects the uterine changes which are necessary for nidation of the fertilized ovum. Failure of the corpus luteum to produce a sufficient amount of its secretion (progestin) would therefore interfere with nidation. Removal of the corpus luteum during early pregnancy results in abortion; hence, a failure of its normal secretion has been considered to be one of the causes of habitual abortion. This is the basis for the use of progesterone in this condition, although the evidence for the efficacy of this form of therapy is still incomplete.

In the human female the corpus luteum degenerates during the later months of pregnacy and the ovaries can be removed without interrupting pregnancy. There is, however, at this period an abundant production of the progestational hormone by the placenta. The latter organ thus takes over the internal secretory function of the ovary as regards the production of both estrogen and the hormone of the corpus luteum.

Our knowledge of the rate of secretion of the progestational hormone is based on a determination of the excretion of pregnandiol. This gradually increases during pregnancy to about 8 mg. per day at the end of the fourth month. After this, there is a precipitous rise to an average of about 40 mg. (10 to 80) per day. Thereafter, there is only a slight rise to a maximum of 20 to 120 mg. at term (average, 50 mg.)[3].

The increase in size and other changes in the uterus during pregnancy are in part probably secondary effects of the gradually increasing bulk of the products of conception, but are also regulated probably by the estrogenic and luteal hormones. The peristalsis of the Fallopian tubes, which propels the ovum into the uterus, and the normal uterine motility during pregnancy and at parturition are also believed to be controlled primarily by these hormones.

The Chorionic Gonadotropin

With the formation of the chorionic villi, there appears in pregnancy a glycoprotein substance variously designated as the anterior-pituitary-like hormone, prolan, cyonin, chorionic gonadotropin, as well as by a number of proprietary brand names. The presence of this substance in the urine is the basis for the Aschheim-Zondek and Friedman tests for pregnancy. The production of this substance may be looked upon as a specific endocrine function of the chorionic tissue, in addition to the production of estrogen and progesterone, which, as we have already seen, is also taken over by the placenta.

The chorionic gonadotropin appears in the urine soon after the first missed menstruation, and increases in amount until it reaches a maximum at the twentieth to the sixtieth day of gestation. At its peak 75,000 to 1,000,000 or more international units may be excreted daily. It then decreases to 1000 units or less per liter, rising slightly during the last month, and disappearing entirely about five days postpartum. The blood level parallels these urinary concentrations. Other tissues related to the chorion (chorionepithelioma, hydatidiform mole, teratoma, seminoma) also produce this hormone.

The exact function of the chorionic gonadotropin in pregnancy is still not clear. Indeed, it can not be said with certainty that it actually performs any physiological function. Of particular interest is the relation

2. Dingemanse, E.; Laqueur, E.; and Muehlbock, O.: Ueber die Ausscheidung oestrogener Hormone in Harn schwangerer Frauen, Monatschr. f. Geburtsh. und Gynaek. 109:-37 (April) 1939.

3. Hamblen, E. C.: Endocrine Gynecology, Springfield, Charles C. Thomas, 1939.

of abnormalities in the production of this substance to pathological states. The Smiths[4] have reported finding high levels in the blood serum during the fifth, sixth or seventh months of pregnancy, and believe that such findings give evidence of an impending eclampsia. In only 12 per cent of their eclamptic patients was this elevation not observed. They claim that excessive amounts are demonstrable in the serum four to six weeks before clinical symptoms are present. Associated with the increased chorionic gonadotropin, there was also observed a relative decrease in the estrogen content of the urine, serum and placenta of toxemic patients. These findings, particularly in diabetic patients, have suggested that an imbalance in the hormones of pregnancy are responsible for toxemic states and that they may be remedied by injections of the appropriate hormones. Confirmation of these claims has, however, not been reported.

Conclusion

Because of the relation of the estrogenic and progestational hormones to the growth, motility and other cyclic changes occurring in the female genital tract during pregnancy, it is tempting to consider abnormalities in the rate of the production of these hormones as the causes of many pathological deviations from the normal, and to attempt to remedy the latter by injection of the appropriate hormone. Unfortunately, in most cases clinical confirmation of these claims has not been made. The sex hormones have been employed for many conditions in which the evidence of their effectiveness is meager.

4. Smith, G. V. and Smith, O. W.: Anterior Pituitary-Like Hormone in Late Pregnancy Toxemia, Am. J. Obst. and Gynec. 38:618 (Oct.) 1939.

Central Nervous System Involvement in Syphilis.—It is now well known that when the central nervous system is involved by syphilis this involvement takes place in the early stage of the infection . . . The majority of the investigations report abnormalities in 25 to 40 per cent of the fluids removed after the appearance of the secondary rash. The very significant conclusion which can be drawn from these studies is not that the cerebrospinal fluid may be involved in the early stages, but that when it remains normal for two or more years after the primary infection it will always remain so and parenchymatous neurosyphilis will never develop.—H. Houston Merritt, M.D.: The Early Clinical and Laboratory Manifestations of Syphilis of the Central Nervous System, New England J. Med. 223:446 (September 19) 1940.

ARACHNODACTYLY (MARFAN'S SYNDROME)

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Arachnodactyly was originally described by Marfan in 1896, and since that date less than 200 cases have been reported in medical literature. This apparent rarity alone may justify the presentation and discussion of a family group in which symptoms of the disease were found; but since, in addition, arachnodactyly was associated with recurrent lymphocytic meningitis in one member of the group, this clinical material may have further value.

Arachnodactyly is probably more common than the number of reported cases would indicate. The multiplicity and insidious development of the symptoms combine to make it of general clinical interest and of particular importance to the pediatrician, the ophthalmologist, the neuropsychiatrist and the orthopedist; for each may be the first to have the opportunity to diagnose it.

Characteristics of Arachnodactyly

Arachnodactyly, variously known as dystrophia mesodermalis congenita, typhus Marfanis, Marfan's syndrome, and dolichostenomelia, is characterized by an elongation of the bony structure, ectopia lentis, weak musculature, and a typical aged physiognomy (fig. 1). These anomalies may be present at birth, but more frequently are first noted following some intercurrent disease, such as measles or influenza, in the early stages of life. Weve, quoted by Burch[1], found the sexes to be equally affected, but there are some authors who believe that it is more common in females.

In the spider-like elongations of the bones of the hand may be found the origin of the name arachnodactyly, first used by Achard in 1902. Burch[1] in his review of 120 cases, reported that the bones show no true pathological change on roentgenological examination. The most striking bony changes are the elongation of the metacarpals and metatarsals; spinal deformity (scoliosis, kyphosis, and kyphoscoliosis), which occurs in about

1. Burch, F. E.: Association of Ectopia Lentis with Arachnodactyly, Arch. Opth. 15:645 (April) 1936.

50 per cent of the cases; the dolichocephalic skull; and the high palatal arch. Ocular abnormalities (dislocated lenses, iridodonesis, high myopia), cardiac involvement in about 35 per cent of the cases, undeveloped musculature with ligamentous relaxation, and lack of subcutaneous fat are all characteristic of the complete picture of arachnodactyly.

It is rare to find a case showing all these types of abnormalities, and the symptoms may appear one by one. The elongation of the bones is often the first sign to be recognized, but the family is not likely to look upon this as a matter requiring medical attention. If a victim develops a marked undernourished appearance, or curvature of the spine, as did one member of the family to be discussed, he may seek treatment. It is more than likely that his illness will be wrongly diagnosed and he will be given nothing more than vitamin extracts and a high caloric diet.

Some degree of spinal deformity has been noted in almost all cases[1,2]. This might conceivably be due to lack of support by the soft parts, but this explanation does not suffice for elongated fingers. When these symptoms are found in conjunction, arachnodactyly should be suspected.

Because the dislocation of the lenses causes most discomfort to the patient, the ophthalmologist is often the first to have the opportunity to diagnose the condition. Although it may not at first be present, ectopia lentis is considered by Lloyd and others to be an integral part of the syndrome. Marfan and Burch report that eye symptoms are observed in some 40 to 50 per cent of cases.

Although unexplained isolated cases do occur[3], it is the general consensus of opinion that arachnodactyly is familial, and that it is inherited according to Mendelian laws. Duke-Elder[4] states that the condition is transmitted as a dominant characteristic, but opinion on this point is not unanimous[5].

There is also some conflict of opinion concerning the effect of arachnodactyly on the mentality. Burch[1] is of the opinion that the mentality is not affected and that the intelligence is frequently of a high order. Lloyd[6], on the other hand, has most frequently found the condition among the feeble-minded, and others[2c, 7, 3b] have reported arachnodactyly in imbeciles and mental defectives.

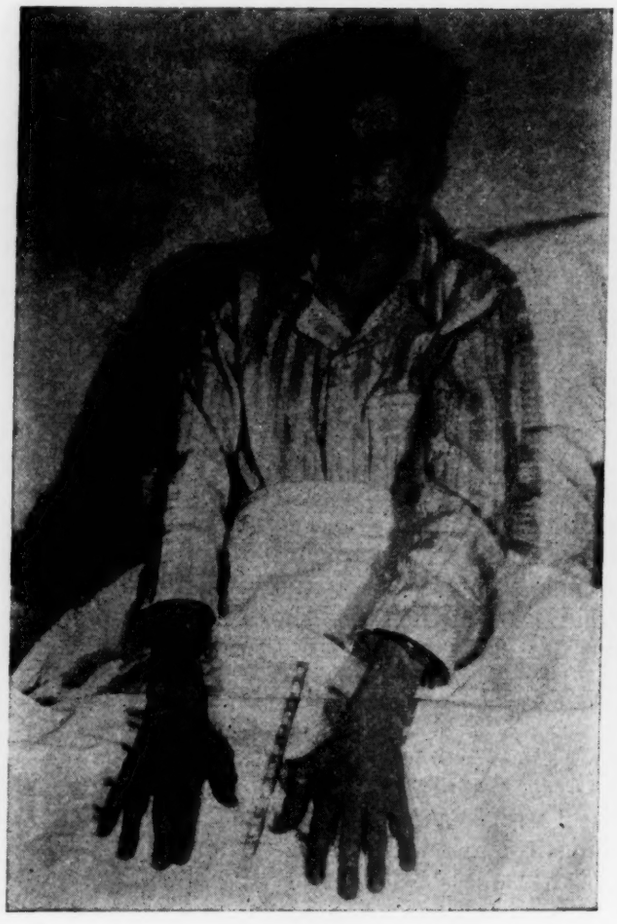

Fig. 1. G. H. at the age of 16.

Case History

G. H. was the youngest of a family of eight, six of whom presented symptoms of arachnodactyly (fig. 2). The disease had apparently been handed down from the mother's side of the family, probably as a prominent Mendelian characteristic. Mrs. H. and four of her nine siblings had some symptoms of arachnodactyly. The maternal grandfather and at least four of his siblings are also believed to have had some features of the syndrome (fig. 3).

G. H. himself was a gangly, poorly developed white male with extremely long fingers

2. (a) Lloyd, R. I.: Arachnodactyly (Dystrophia Mesodermalis Congenita, Typhus Marfanis; Marfan's Syndrome; Dolichostenomelia), Arch. Ophth. 13:744 (May) 1935.
(b) Olcott, C. T.: Arachnodactyly (Marfan's Syndrome) With Severe Anemia, Am. J. Dis. Child. 60:660 (Sept.) 1940
(c) Pino, R. H.; Cooper, E. L.; Van Wien, S.: Arachnodactyly and Status Dysraphicus. A Review, Ann. Int. Med. 10:1130 (Feb.) 1937.
3. (a) Moore, T. I.: Arachnodactyly, Arch. Ophth. 21:854 (May) 1939.
(b) Stewart, R. M.: A Case of Arachnodactyly, Arch. Dis. Childhood 14:64 (March) 1939.
4. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby, 1938, v. 2, p. 1352.
5. Harrison, J. and Klainer, M. J.: Arachnodactyly: Its Occurrence in Several Members of One Family, New England J. Med 220:621 (April 13) 1939.
6. Lloyd, R. I.: A Second Group of Cases of Arachnodactyly, Arch. Opth. 17:66 (Jan.) 1937.
7. Rambar, A. C. and Denenholz, E. J.: Arachnodactyly, J. Pediat. 15:844 (Dec.) 1939.

Fig. 2. Family group. G. H. is fourth from the right and E. H. is second from the left.

and toes and a peculiar but typical physiognomy (fig. 1). Some characteristics of Marfan's syndrome, such as the elongated bones and weak muscles, were already well demonstrated in him at the age of 6, when he was referred to me with his first attack of lymphocytic meningitis; then their significance was not recognized, however, and the eye signs were not present. It was on his second visit, ten years later, that examination revealed ectopia lentis of both eyes; this finding in conjunction with the other characteristics led to the diagnosis of arachnodactyly and to a decision to investigate his family background.

At the age of 16 G. H. presented the undeveloped, ill nourished appearance which is characteristic of arachnodactyly and is the product of the combined effect of lack of subcutaneous fat and poorly developed musculature. Perhaps the most striking feature of his case, however, was the characteristic development of the bony structure. Beginning life as an apparently normal baby, he developed a dolichocephalic skull, and the bones of his hands and feet became abnormally elongated as he grew older (fig 1). This elongation did not seem to have resulted directly from any intercurrent infection. The only history of possible infection during his sixteen years was that of chronic tonsillitis preceding tonsillectomy performed at the age of 14. It is more than likely that his tonsils were removed in an attempt to benefit his general health.

The unusual elongation of the bones had first been noted when he was about 4 years old, and had progressed in the succeeding years. This was the symptom most noticeable in his mother and other relatives, who apparently had less pronounced arachnodactyly. His arms and legs were elongated, as well as his hands and feet, and he had a rachitic deformity to the right of the sternum. He has not, at the present date, developed spinal curvature, but this may yet follow. His sister, E. H., aged 23, in whom the symptoms are developing in different order, had a right dorsal left lumbar scoliosis of the spine, with no compensatory curve, and a heart thrill due to endocarditis. A two stage fusion operation was done for the scoliosis in 1938 and 1939. Following the second operation there was an almost fatal heart failure. A back brace was prescribed for the

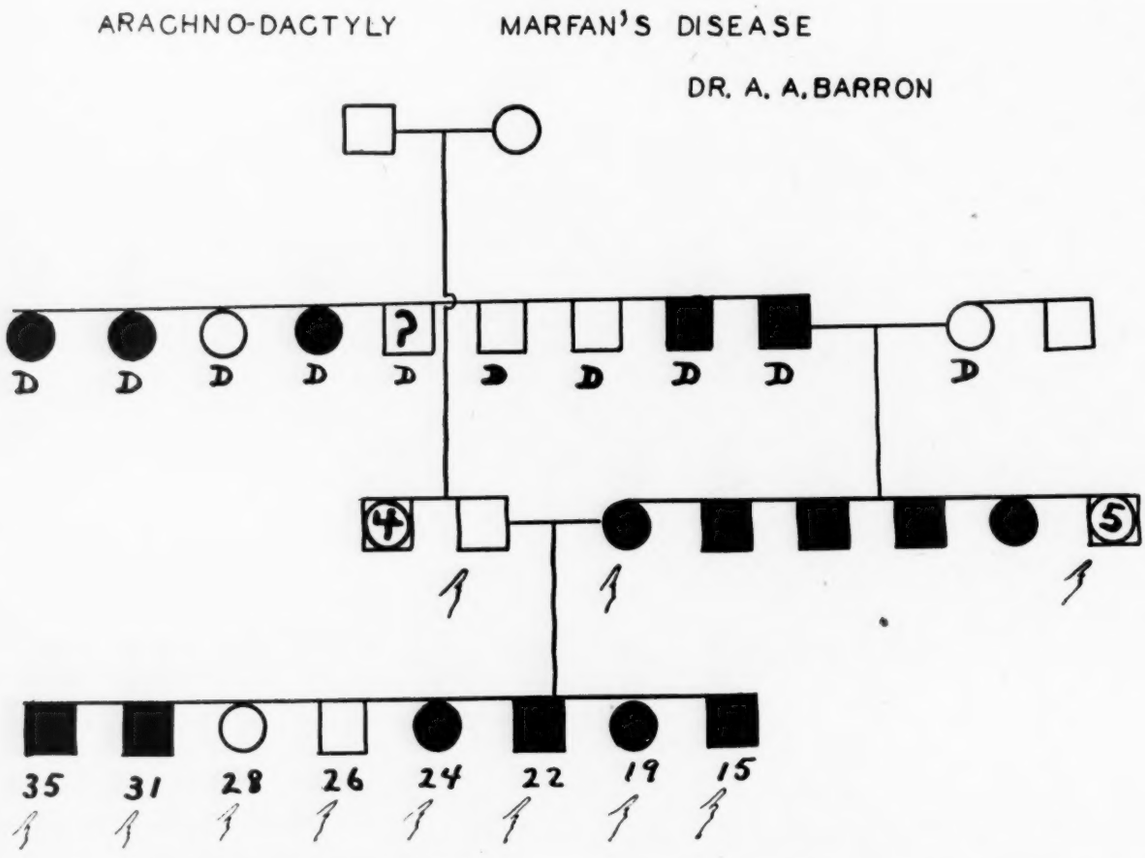

Fig. 3. Pedigree by Dr. William Allan
Squares indicate males, circles females.
Black squares and circles indicate members showing symptoms of arachnodactyly.
Pointing hand indicates members examined.

pseudo-arthritis which developed between the two fused areas. At that time it was not suspected that her condition was due to arachnodactyly.

In the case of G. H. there was no cardiac involvement, as is so often recorded, and except for a to and fro friction rub over the apex the heart appeared to be normal. Time will show how far muscular weakness may affect his heart; for death from cardiac involvement, at an early age, is often the terminal stage of arachnodactyly. However, various factors affect the prognosis, and it appears that characteristic symptoms which develop fatally in one case may lie comparatively dormant in another. If the patient does not ultimately succumb to a heart disorder, the general weakness often predisposes to pneumonia and other infections. G. H.'s lungs were negative for pathologic lesions, and the liver, kidneys, and spleen were not palpable. The sella turcica was normal. The basal metabolism was minus 5.

The eye symptoms which had developed in the interim between his sixth and sixteenth years were characteristic. Ophthalmological examination by Dr. Frank Smith revealed unusual eye grounds with ectopia lentis of both eyes; the fundi were difficult to see because of the dislocated lenses, and there was stretching suggesting myopia. This is a perfect picture of the signs of arachnodactyly, and the diagnosis was suggested by Dr. Frank Smith. Four of G. H.'s siblings were also found to have dislocated lenses.

While the findings here noted are undoubtedly those of arachnodactyly, G. H. at this second visit also had symptoms of lymphocytic meningitis—that form of meningitis characterized by an acute onset, a benign course, and a high lymphocyte count of the spinal fluid[8]. The onset of this second attack (which has been reported and discussed in a previous paper[9]) was accompanied by the typical symptoms and signs of headache, nausea and vomiting, nucal rigidity, a positive Kernig's sign, a suggestive Babinski reaction, and a slight elevation of temperature.

8. Skogland, J. E.: Benign Lymphocytic Meningitis, Minnesota Med. 22:462 (July) 1939.
9. Barron, A. A.: Lymphocytic Meningitis, North Carolina M. J. 3:125 (March) 1942.

Superficial and deep reflexes were present, but the deep reflexes were of low amplitude. Spinal fluid examination revealed a leukocyte count of 996, with 80 per cent lymphocytes; there were no tubercle bacilli and the Wassermann reaction was negative. Instructions were given to make a search for the virus of Armstrong and Lillie[10], which has been shown to be present in some cases of lymphocytic meningitis; but owing to an unfortunate misunderstanding the instructions were not carried out.

While the acute meningeal symptoms abated under treatment, this boy has had frequent recurrences of occipital and frontal headaches such as he had in the ten years between his acute attacks and previous to his first attack. These persistent signs of meningeal irritation are curiously inconsistent with the usual reports of the outcome of lymphocytic meningitis, and may suggest that this boy has a chronic disorder of the nervous system paralleling his chronic under-nourishment and poor development.

Etiology

The etiology of arachnodactyly is still in the realm of theory. The problem of finding one plausible explanation linking together undeveloped musculature, nervous disorders, ocular abnormalities, and elongated bony structure without pathological changes is not an easy one. Explanations for each separate and individual phenomenon may be found in persons not having arachnodactyly, but a theory which may plausibly link together the phenomena in the syndrome has not yet been found. There have been regrettably few autopsies reported.

Early theories suggested as possible causes mongolism and endocrine, metabolic, pituitary and parathyroid disturbances. In view of the familial occurrence it is now most generally accepted that the basis of abnormalities is laid in intra-uterine life, as a result of defects of the germ plasm, faulty closure of the neural tube (Passow), or toxic disturbances affecting the development of the mesoderm and even of the ectoderm.

Dr. Ida Mann[11] has postulated two ways in which the various factors may be linked. She points out that "various factors may account for the linking of defects. In the first place, the defect may be in certain chromosomes. Since the chromosomes carry many genes mediating different characters in various tissues, it is to be expected that superficially unrelated characteristics may be found to be related by their genic position in the blastomeres. There is not evidence to lead us to suppose that mesodermal and ectodermal structures are segregated in different chromosomes." She points out that there is evidence that the same chromosomes may carry character for the eyes and for the extremities.

In this connection it might be interesting to note that Lloyd records that all his patients had dark hair, a fact which suggests that the genes affected were carried in the chromosomes mediating dark hair. On the other hand, with the exception of one German, all of Lloyd's patients were of Jewish or Italian parentage, which would account for the coloring and might only show us that arachnodactyly has a geographical or racial distribution.

Dr. Mann also points out that if the defect is not genic but is due to toxic or endocrine disturbances acting at a later date "there is nothing inherently improbable in such a condition affecting both mesodermal and ectodermal structures alike, since the action of toxins during development is specific, not for the toxin, not for a given tissue, but for the period of development at which it begins to act and for those structures which are undergoing most rapid differentiation."

Dr. Mann's two theories provide a plausible explanation of the linkage of the oft-recognized abnormalities, and of the neurological symptoms described in this paper.

Neurologic and Psychiatric Aspects of Arachnodactyly

The case of G. H. has unusual features which might suggest that arachnodactyly, in addition to its oft-noted effects upon the bony structures and the musculature, may involve to some extent the nervous system.

This is not an original suggestion, although the supporting facts are of a new type. In 1927 Moro[12] drew attention to what he believed to be a neurological type of the disease, in which hyperreflexia, foot clonus, nystagmus, and a positive Babinski

10. Armstrong, C. and Lillie, R. D.: Experimental Lymphocytic Chorio-Meningitis of Monkeys and Mice Produced by a Virus Encountered in Studies of the 1933 St. Louis Encephalitis Epidemic, Pub. Health Rep. 49:1019 (Aug. 31) 1934.

11. Mann, Ida: Personal communication to Burch.

12. Moro: Ueber die Neurologischen Form der Arachnodactylie Meunchen Med. Woch. 74:1071, 1927.

sign were present. His ideas met with criticism, and it was suggested that these signs were but the product of weakness and physical exhaustion. To this criticism he replied that although general weakness might conceivably bring about some of the symptoms, the positive Babinski could not be explained on this basis.

In the case of G. H., with a family background threaded through with arachnodactyly, it is difficult to escape the suggestion that his neurological ill-health, evinced by two attacks of acute lymphocytic meningitis, with chronic meningeal symptoms during the intervening ten year period, might be linked with the familial Marfan's syndrome.

There are a few reports of cases of arachnodactyly in which neurologic or psychiatric symptoms were recorded. J. D. Fahey[13] described a case of arachnodactyly in a girl aged 15 who "came to the clinic because of frequent attacks of headache." (He does not elaborate this finding but proceeds to delineate the other characteristics which led to a diagnosis of arachnodactyly.) It is possible that the headache might have been the result of defective eyesight, but it should be noted that the patient had worn glasses since the age of 6 years, and there is no suggestion that the glasses were inadequate for her requirements.

Fahey reported a second case of arachnodactyly with possible neurological symptoms in a man aged 45, who "was seen because of pain in suboccipital region, loss of memory and spots before the eyes." Four years previously the patient had had a hemorrhage in the right retina, following which the vision had become defective on that side. He had had "intermittent pain from the right frontal to the occipital region"—a type of headache which resembles the chronic meningeal headache of G. H. In Fahey's case, the pains four years earlier might have been due solely to the eye involvement, but it is still open to question whether all headaches at later dates were due to visual defect alone, especially in view of the fact that the patient also complained of loss of memory.

Burch, in his review of 120 cases of arachnodactyly, states that the nervous system and mentality are not affected "as a general rule". Among his own 8 cases there was one —that of a boy aged 10—in which the ankle and knee jerks were absent on the right side and sluggish on the left. The boy had had at the age of 3 years an attack of "doubtful" infantile paralysis, followed by chicken pox at 5 and measles at 9. "He did not talk until he was three."

In addition to these cases of arachnodactyly in which there may have been some neurological involvement, there have been reported cases associated with mental disorders. Pino, Cooper and Van Wien[2c] reported a case in a boy of 8 years, and stated that "it was impossible to ascertain the vision in the usual way due to poor mentality." Psychological examination led to the conclusion that there was cerebral maldevelopment. The authors noted that although the boy was obviously defective mentally his mental reactions improved when he was fitted with glasses. The same authors reported a case of arachnodactyly in a boy aged 20, who had been "operated upon several times for meningeal adhesions to relieve epileptic attacks," and Stewart has reported a case in a male epileptic imbecile, aged 16, but with a mental age of 5 years. In the evaluation of these cases with apparent mental retardation it is always necessary to remember the handicap of poor eyesight to perceptive learning. Moore[3a] reports "dramatic results" in improved school work when a boy with arachnodactyly was supplied with suitable glasses.

Probably the most interesting contribution to our knowledge concerning neurologic and psychiatric symptoms was provided by Lloyd in his second paper on this disease[6], in which he added 9 cases to 5 previously reported. One patient, a boy of 15 years, the offspring of a marriage between a woman and her uncle, was "suspected of being mentally defective", and a second patient, a boy who grew to a height of 6 feet, 8½ inches, had "some indications of increased cerebral pressure." In this paper Lloyd states definitely that dislocation of the lense "had been found to be more frequent among young inmates of institutions for the feeble-minded" than in the general population. In such cases the skeletal defects may have been present, but have not always been mentioned.

This statement concerning the incidence of ectopia lentis in institutions for mental defectives suggests two possibilities. One is that many cases of arachnodactyly are unreported because they are hidden away in such institutions; and that these patients are more likely to have neurological symp-

13. Fahey, J. J.: Muscular and Skeletal Changes in Arachnodactyly, Arch. Surg. 39:741 (Nov.) 1939.

toms, similar to those of G. H. The other possibility is that not all patients with dislocated lenses in these institutions are actually mental defectives, but that some may be retarded in perceptive learning by defective vision (as in Moore's case[3a]). If the symptoms of arachnodactyly are sought for and recognized, and the patient is examined by an ophthalmologist for displaced lenses, these cases might be removed from the ranks of the alleged feeble-minded. Certainly children who have difficulty in reading should have the advantage of a careful eye-ground examination.

Summary

The characteristics and etiology of arachnodactyly have been discussed and its occurrence in several members of a family group has been reported. The mother and six of her children showed the characteristic elongated bony structure. Four of the siblings had ectopia lentis. Of these four, one had a left lumbar scoliosis of the spine, while another, G. H., had had two acute attacks of lymphocytic meningitis and some chronic symptoms which might seem to indicate involvement of the central nervous system. There is no proof that this simultaneous occurrence of meningeal and arachnodactylous symptoms was a coincidence or that the two chronic conditions were linked in a close association. The case is recorded in the hope that it may add to the sum of knowledge concerning the possible lines of development of arachnodactyly.

An attempt is made to show the various orders in which symptoms may develop in different individuals. It is suggested that the pediatrician, the orthopedist and the ophthalmologist, in addition to the internist and the neuropsychiatrist, should be on the look-out for symptoms of arachnodactyly so that patients may not be unsatisfactorily treated for isolated clinical symptoms such as malnutrition, spinal curvature or apparent mental deficiency.

The writer gratefully acknowledges the constructive help of Dr. Frank C. Smith and Dr. William Allan, both of Charlotte, Dr. W. K. McGill of Clover, S. C., and Dr. L. A. Coleman of Spartanburg, S. C.

Routine collapse therapy of minimal pulmonary tuberculosis is not justified. Conservative therapy is the treatment of choice. From 75 to 80 per cent of the cases (studied) resolve or fibrose and become stable with bed-rest and remain well. I. D. Bobrowitz, M.D., Amer. Rev. of Tuber., Mar., 1942.

A NOTE ON SOME EXPERIMENTAL RESULTS SUGGESTING THE USE OF SODIUM PHENTETIOTHALEIN IN THE TREATMENT OF ENTERIC INFECTIONS OF BACILLARY ORIGIN

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The literature of the past two decades is replete with methods of treating the acute and chronic enteric infections of bacillary origin, particularly those of the typhoid-paratyphoid-dysentery group. All earlier attempts at specific therapy in the acute infections were unsatisfactory and offered no more than the usual supportive measures. In 1933 Browning[1] reviewed every method available of dealing with the chronic enteric carrier and considered them all inadequate.

The experimental work upon which this note is based was carried out in 1935. The results were then thought to have little significance and were not reported. Since that time, clinical evidence brought forth elsewhere seems to justify a brief presentation of this material for whatever value it may now possess.

Soluble iodophthalein was first used in the treatment of typhoid carriers by Onodera and his co-workers[2] in 1931. Seven proven carriers were treated with one or two doses of this drug intravenously, followed by irradiation of the gallbladder. Three patients showed persistently negative stool, urine and bile drainage cultures during the next month, at the end of which time observation was terminated. Two patients had temporarily negative cultures and two were not affected. The authors declared that the drug was ineffectual in acute typhoid fever. Oral administration of the dye was also unavailing in their patients. They studied the sterilizing power of soluble iodophthalein on Eberthella typhi *in vitro*, and reported convincing results. Exposure to roentgen rays did not enhance the bactericidal quality of the dye

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1. Browning, C. H.: Chronic Enteric Carriers and Their Treatment, Medical Research Council, Special Report Series, No. 179, London, His Majesty's Stationery Office, 1933.

2. Onodera, N.; Murakawa, G.; and Liu, S.: Ueber eine neue Behandlung von Typhusbazillentraegern, Deutsches Arch. f. klin. Med. 171:503, 1931.

under these conditions. However, the authors considered irradiation of the gallbladder after administration of the dye to be necessary to a maximal bactericidal action. They emphasized the fact that at least a temporary sterilizing effect was always reflected in the stool cultures.

Saphir and Howell[3] in 1940 gave soluble iodophthalein orally to 1 paratyphoid A carrier, whose stool cultures then became negative and remained so throughout a seven months' follow-up period. They considered oral administration of the drug more efficacious than intravenous administration, both for concentration in the gallbladder and for local action in the intestine. Their studies were supplemented by experiments in which a bile solution containing 4 to 6 per cent of the dye was shown to be bactericidal for Salmonella paratyphi *in vitro* after ten hours' contact. These results approximated those of Onodera and his coworkers, who found that a 4 per cent solution killed the organisms within twelve hours and a 6 per cent solution within three hours.

Enright in 1941[4] treated a confirmed typhoid carrier with oral soluble iodophthalein and demonstrated an immediate disappearance of the pathogen from the stools. Later stool cultures were not reported.

New interest in the therapeusis of enteric fevers was aroused by the introduction of sulfonamide compounds. Marshall and others[5] employed sulfaguanidine with promising effect in the management of bacillary dysentery in children. Rantz and Kirby[6] likewise reported encouraging results with the same drug in dysentery carriers. Earlier, Levi and Willen[7] had used sulfaguanidine with apparent success in a typhoid carrier. Cutting and Robson[8], on the other hand, have recently disclaimed the efficiency of a great variety of agents in the treatment of typhoid carriers. Their investigations dealt with phenothiazine, phenothiazone, thional, soluble iodophthalein, sulfanilamide, sulfathiazole, sulfadiazine and sulfaguanidine. Each of these drugs in a 0.1 per cent concentration failed to influence the growth of the typhoid organism *in vitro*. They also employed phenothiazine, thional, soluble iodophthalein, sulfadiazine and sulfaguanidine in the treatment of 6 typhoid carrers and 1 dysentery carrier without success.

At the moment, then, there is a confusing diversity and uncertainty of opinion regarding chemotherapeutic methods applicable to the enteric fevers. The following data are intended to be in no way controversial.

Experimental Data

Experiments were designed to test the bactericidal power of soluble iodophthalein and related compounds against E. typhi *in vitro* and to ascertain the bactericidal activity and quantity of the dye that could be concentrated in the gallbladder of an experimental animal. Four of the commercial halogen derivatives of phenolphthalein were selected — namely, the disodium salts of phenoltetrabromphthaleinsulfonate (bromsulfalein), phenoltetrachlorphthalein, tetraiodophenolphthalein (soluble iodophthalein) and phenoltetraiodophthalein (sodium phentetiothalein). These compounds are fully described in NEW AND NONOFFICIAL REMEDIES, 1940. The solution strength of each drug tested was based upon average dosage and the estimated dilution of the drug in the hepatobiliary and intestinal tracts of man

The bromine compound was shown to exert the least bactericidal effect of any of the dyes employed. The chlorine derivative, on the other hand, was found to be the most effective by a small margin, weight for weight, since a 1 per cent solution of the drug killed typhoid bacilli in less than an hour after contact. However, the toxicity of this compound invalidated its advantages. It was decided that only soluble iodophthalein and sodium phentetiothalein possessed any practical value as bactericides because they could be administered safely in large doses. The essential experimental data regarding these preparations are given below.

Tubes containing 5 cc. portions of sterile solutions of each dye in varying strengths were inoculated with 0.5 cc. of a twenty-four hour broth culture of E. typhi of known virulence, and were incubated at 38 C. A loopful of each inoculated solu-

3. Saphir, W., and Howell, K. M.: Soluble Iodophthalein in Treatment of Carriers of Typhoid-Paratyphoid Group, J. A. M. A. 114:1988, (May 18) 1940.
4. Enright, J. R.: Apparent Cure of a Typhoid Carrier with Soluble Iodophthalein, J. A. M. A. 116:220 (Jan. 18) 1941.
5. Marshall, E. K.; Bratton, A. C.; Edwards, L. B.; and Walker, E.: Sulfanilylguanidine in Treatment of Acute Bacillary Dysentery in Children, Bull. Johns Hopkins Hosp. 68:94 (Jan.) 1941.
6. Rantz, L. A., and Kirby, W. M. M.: The Use of Sulfaguanidine in the Treatment of Dysentery Carriers, J. A. M. A. 118:1268 (April 11) 1942.
7. Levi, J. E., and Willen, A.: The Typhoid Carrier State Treated With Sulfaguanidine, J. A. M. A. 116:2258 (May 17) 1941.
8. Cutting, W. C., and Robson, G. B.: The Alleged Efficiency of Medical Treatment of Typhoid Carriers, J. A. M. A. 118:1447 (April 25) 1942.

tion was then transferred into a tube of beef infusion broth (pH 7.4) at intervals up to twenty hours. These tubes were incubated at 38 C. for twenty-four hours and were then examined for growth. The results (growth indicated by X, no growth by —) were as follows:

Soluble iodophthalein in distilled water

		2%	4%	6%	7%	8%	Control
Hours of contact of organism with dye	1	X	X	X	X	X	X
	2	X	X	X	X	X	X
	3	X	X	—	—	—	X
	4	X	X	—	—	—	X
	5	X	X	—	—	—	X
	6	X	X	—	—	—	X
	20	X	X	—	—	—	X

Soluble iodophthalein in neutral ox bile

		2%	4%	6%	7%	8%	Control
Hours of contact of organism with dye	1	X	X	X	X	—	X
	2	X	X	—	—	—	X
	3	X	X	—	—	—	X
	4	X	X	—	—	—	X
	5	X	—	—	—	—	X
	6	X	—	—	—	—	X
	20	X	—	—	—	—	X

Sodium phentetiothalein in neutral ox bile

		1%	1.5%	2%	2.5%	3%	Control
Hours of contact of organism with dye	1	X	X	X	X	—	X
	2	X	—	—	—	—	X
	3	X	—	—	—	—	X
	4	X	—	—	—	—	X
	5	X	—	—	—	—	X
	6	X	—	—	—	—	X
	20	X	—	—	—	—	X

It was evident that the presence of ox bile increased the effectiveness of soluble iodophthalein against **E. typhi.** However, sodium phentetiothalein in neutral ox bile solution had a distinctly greater lethal effect.

An attempt was now made to determine the bactericidal power and concentration of sodium phentetiothalein as stored in the gallbladder of an experimental animal. Six rabbits and three cats were utilized in these procedures. Roentgenographic studies of dye concentration, however, soon revealed that the cat was superior to the rabbit for this purpose. Results were uniform; the following is representative:

A 4500 Gm. cat, starved for twenty-four hours prior to and throughout the experiment, was anesthetized with nembutal, and 1.5 cc. of a sterile 8 per cent solution of sodium phentetiothalein was injected into the femoral vein. Two more injections of 2 cc. each were given forty-eight and seventy-two hours later. At ninety-six hours, a roentgenogram showed the gallbladder well filled with dye. The cat was sacrificed and 2.5 cc. of bile were withdrawn from the gallbladder under aseptic precautions. The bile was yellowish brown and exhibited none of the characteristic purple color of phentetiothalein in solution. The dye had been decolorized by the acid reaction of the bile and was found to be incapable of killing typhoid bacilli **in vitro** even after seventy-two hours' contact. A 5 per cent aqueous solution of sodium phentetiothalein was prepared and treated with 0.1 normal hydrochloric acid until it was decolorized. The resulting material likewise failed to affect the growth of the organism.

The concentration of dye in the recovered bile was determined colorimetrically. One-half cubic centimeter of bile was cleared by adding lime water and allowing the mixture to stand. The supernatant fluid, now a deep purple, was withdrawn, filtered, and diluted with 0.1 normal sodium hydroxide until 30,000 parts of the dilution represented one part of recovered bile. A standard was prepared by diluting one part of a 1 per cent aqueous solution of sodium phentetiothalein with 20,000 parts of 0.1 normal sodium hydroxide. The standard and unknown solutions matched closely at these ratios. The recovered bile, therefore, had contained decolorized dye in a concentration of approximately 1.5 per cent.

Discussion

The bacteriological results given above are comparable to those of Onodera and his co-workers, and Saphir and Howell in regard to soluble iodophthalein. However, sodium phentetiothalein is shown to be an even more effective bactericide for E. typhi *in vitro.* This might be due to the fact that the iodine content of sodium phentetiothalein lies between 56 and 59 per cent, while that of soluble iodophthalein is approximately 53 per cent. The clinical dose of both is the same (4 Gm. orally, or 40 mg. per kilogram of body weight intravenously). Weight for weight, sodium phentetiothalein is the less toxic of the two and is therefore tolerated in greater dosage. Both dyes dissolve readily in aqueous solution at a pH of 7 to 9. When the hydrogen ion concentration exceeds this limit, they are decolorized and form an insoluble, milky precipitate. In sufficiently strong solution, both destroy the typhoid organism; decolorized, they have no effect whatever.

The presence of bile definitely enhances the bactericidal effectiveness of soluble iodophthalein, in spite of the fact that bile is known to favor the growth of the typhoid organism. The reason for this is not clear. It is possible that bile has an oxidizing effect on the dye, liberating iodine, or that it plays some intermediate role in the reaction between dye and organism.

Sodium phentetiothalein is well concentrated in the gallbladder of the cat, although it is decolorized by the acid reaction of the bile and becomes innocuous to the typhoid bacillus. This fact may explain, in part, the variability of the results reported in the treatment of typhoid carriers with soluble iodophthalein.

It has been estimated that, by oral or intravenous administration, the dye may reach a concentration of 8 per cent in the normal human gallbladder. This amount should be more than adequate to sterilize gallbladder contents infected with E. typhi, provided the hydrogen ion concentration remains favor-

able and keeps the dye in solution. Whether such ideal conditions could obtain would certainly depend upon the functional capacities of the hepatobiliary system and intestine and upon the acid-base balance of the body as a whole.

In view of the fact that a degree of success has already been demonstrated in the use of soluble iodophthalein for the treatment of enteric carriers, a modified chemotherapeutic approach might be proposed in the light of data presented above. Sodium phentetiothalein, instead of soluble iodophthalein, would be the drug of choice. A combination of oral and intravenous administration probably should be most effective, with dosage repeated according to individual limits of intoxication. At the same time, an attempt could be made to keep the dye from being decolorized in the biliary tract and intestine by instituting a regimen of systemic alkalinization. In certain cases, a solution of the drug might be introduced directly into the intestine through a duodenal tube. Intestinal and biliary stasis should be encouraged in order to prolong contact of organisms with dye and to counteract the drug's laxative effect. A low-residue, low-fat diet and small doses of camphorated tincture of opium could be employed to this end.

It is hoped that the foregoing statements may promote continued interest in the subject. Certainly an effort should be made to ascertain the efficacy of the dye administered to infected animals under the proposed conditions. The practicability of the suggested therapeutic plan, however, can be determined only by careful clinical trial in patients with acute enteric infections as well as in carriers.

Summary

1. Experimental data are presented to show that sodium phentetiothalein in neutral ox bile solution is bactericidal for E. typhi *in vitro* in higher dilutions than is soluble iodophthalein.
2. The presence of ox bile increases the effectiveness of soluble iodophthalein against E. typhi *in vitro*.
3. If a bactericidal solution of sodium phentetiothalein is acidified with dilute hydrochloric acid until decolorized, it is rendered innocuous to E. typhi *in vitro*.
4. Sodium phentetiothalein is concentrated in the gallbladder of the cat as a decolorized compound. If converted into its soluble form, it is present in strength sufficient to kill E. typhi *in vitro*.
5. A modified method for the treatment of acute and chronic enteric infections of bacillary origin is proposed. This calls for the administration of sodium phentetiothalein orally and intravenously, with repetition of the dose within individual limits of intoxication, and with systemic alkalinization and the encouragement of biliary and intestinal stasis.

The Significance of Names—As physicians, pay attention to words and names; they are of deeper significance than you might think. Not infrequently the name by which a disease is known carries within itself the seeds of gross errors of thought. "Exophthalmic goitre," for example, with its false implication that exophthalmos is of great importance in the syndrome of thyrotoxicosis; or "amebic dysentery," which completely overlooks the many instances of amebiasis, which develop liver abscess without any dysentery whatever; or, again "tropical sprue," which emphasizes latitude, a fact of little importance, instead of dietary habits, which are all-important.

Someone has pointed out that man is the only animal who creates gods; the medical species of **Homo sapiens** might be defined with fair accuracy as the animal who creates names! Many writers harbor the puerile notion that coining a new name, even a nonsensical name, advances in some mysterious way our knowledge of the disease. Take sprue, for example; it is variously referred to as Celiac Disease, Chronic Intestinal Indigestion, Psilosis, Gee-Herter Disease, Gee-Herter-Thaysen Disease, Hill Diarrhea, Idiopathic Steatorrhea, etc. It is true that the word "sprue," meaning "aphthous stomatitis," is inadequate, but it is unpretentious, has the sanctity of age and priority, and does not conceal ignorance behind such an empty, bombastic phrase as "Idiopathic steatorrhea." Regard with suspicion the man who seeks refuge in polysyllables; a thing clearly understood can always be expressed in simple terms.—Hanes, Frederic M.: Meningococcus Infection, Internat. Clin. v. 3, series 48, p. 261, 1938.

Psittacosis.—A few words should suffice to summarize the diagnosis and treatment of psittacosis. It is a typhoid-like illness with pneumonia, seen among families who have recently acquired new bird pets. We suggest further trial of sulfapyridine or other chemotherapy.—H. C. Hinshaw: Psittacosis: Possible Response to Sulfapyridine, Proceedings of the Staff Meetings of the Mayo Clinic, 15: 662 (October 16) 1940.

Depression.—When a patient is depressed and apparently exhausted without obvious cause, when two or three overhaulings have failed to reveal any organic disease, and when one or more near-relatives have suffered with melancholia, the physician should begin to suspect that the trouble is a mild depression. — Walter C. Alvarez: What's Wrong With the Patient Who Is Always Tired?, Minnesota Medicine, 23:788 (November) 1940.

THE INHERITANCE OF CERTAIN VARIETIES OF MENTAL DEFECT

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and
SIDNEY L. HALPERIN

In contemplating the unconquered diseases that scourge the world, such as yellow fever and trachoma, we are accustomed to look forward to the discovery of cause and cure. But in examining the causal factors operative in the many varieties of mental deficiency we can hope at present only for prevention, since cure seems beyond the bounds of reasonable expectation in most instances. While the hereditary factor in mental defect has yet to be fully explored, recent research would indicate that the solution for at least a small part of this problem may lie in the field of genetics. Where mental deficiency is caused by the action of pathological genes present in one or both of the original cells, and may thus continue to be inherited from generation to generation, a knowledge of the mode of inheritance may throw considerable light upon the possibilities for the prevention of such defects in the population.

The congenital entity of *mongolism* has long been recognized, but its cause still remains unknown. The incidence of this condition in the population is not accurately known, but it has been estimated to occur more frequently than once in 10,000 of the population. This estimate may be five or even ten times too low, because many cases are not recognized and a high percentage of these children die before they reach puberty. It is likely that in the state of North Carolina there are more than 500 mongols, perhaps almost 1000.

Since mongolism is present at birth it has inspired careful genetic study, which has yielded very interesting results. It is significantly familial—that is, it may occur in more than one sibling; and it is found more frequently among relatives of the affected than chance occurrence would permit. The likelihood of a genetic etiology is further suggested in studies of twin mongols, which show that identical twin pairs are usually both affected. This is not the case among fraternal twins. On the whole, the evidence is that some genetic factor, as yet unknown, is involved. Many genes are known whose expression may be incomplete or a matter of degree. The genetic factor in mongolism is an example of this type. Mongolism is also an excellent example of the subtle interrelationship and interdependence of heredity and environment. Every trait or character, be it normal or pathological, is the product of the influences of variation in *both* heredity (nature) and environment (nurture). The evidence is unmistakable that lateness of childbearing is a significant environmental influence in mongolism. It is to be noted that it is the mother's age which is important, and not the number of children she has had. The father's age is not a factor. It has been shown that if childbearing were restricted to the period between 20 and 30 years of age, mongolism would occur at only one-fourth its present rate. Many physicians still regard mongolism as a defect in thyroid function, but recent studies[1] have indicated that this is not so.

The European physician Folling recently discovered[2] that from 1 to 2 per cent of idiots in a certain institution for mental defectives excreted in their urine phenylpyruvic acid, which is a product of the incomplete oxidation of the protein constituent phenylalanine. Dr. L. Penrose of England, who was carrying on research into the causes of mental deficiency at the time, became interested in the problem. In studying the families of patients with this condition he soon discovered, to his surprise, that no mentally normal individual in such families excretes this abnormal metabolite. After making exhaustive studies, he found[3] that about one-fourth of the siblings in such families are idiots and have the same metabolic abnormality. The condition is now known as *phenylketonuria*. It is due to the action of a single recessive gene, a fact which has been verified in our own country by Jervis[4]. Here is an abnormality in body metabolism which is caused by the action of a gene and which is associated with mental deficiency. Of added interest is the fact that

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2. Folling, A.: Ueber Ausscheidung von Phenylbrenztraubensauere in den Harn als Stoffwechselanomalie in Verbindung mit Imbezillitaet, Ztschr. f. physiol. Chem. 227:169, 1934.
3. Penrose, L. S.: Two Cases of Phenylpyruvic Amentia, Lancet 1:23 (Jan. 5) 1935.
4. Jervis, G. A.: Inherited Biochemical Alterations in Certain Types of Mental Deficiency, Proc. Am. A. Ment. Deficiency (no 2) 61:101, 1937.

Dr. Penrose has very recently been able to show[5] that peripheral nerve tumors may be found in some of these cases.

A severe abnormality in lipoid metabolism which is associated with mental deficiency is a condition called *gargoylism.* It was described as far back as 1908. Hunter in 1917 and Hurler in 1919 recognized this peculiar syndrome and regarded it as a new disease. In 1936 Ellis, Sheldon, and Capon[6] reviewed the literature and presented a series of cases of their own. They suggested the name gargoylism. In 1937 Ashby, Stewart, and Watkin[7] described the pathologic changes involved. They discovered that the neuropathologic lesions were strikingly similar to those found in juvenile amaurotic idiocy. In 1938 Kressler and Aegerter[8] demonstrated widespread extracerebral deposits of lipoid in some of the tissues they examined.

The clinical picture in gargoylism is characterized by abnormalities of the osseous system, congenital clouding of the corneas, abdominal distention with enlargement of the liver and spleen, and the presence of marked mental deficiency. A careful statistical analysis[9] of the cases reported to date yields evidence that this condition is similarly due to the action of a pathological gene, recessively inherited. Thus it has again been possible, by means of genetic analysis, to throw light upon a syndrome in mental deficiency which until now was classed as "undifferentiated". Among the four other lipoidoses which fit into the group of congenital disorders (Gaucher's disease, Schuller-Christian disease, Niemann-Pick disease, and Tay-Sachs disease) the familial incidence is rather high, and there is some evidence that these diseases may be similarly inherited. Tay-Sachs disease, or juvenile amaurotic idiocy, is known to be due to the action of a gene which is recessive. This condition is characterized by a history of progressive blindness with subsequent mental and physical deterioration. The incidence of this condition is about 4 per 100,000 births.

We have recently seen a patient with a rare anomaly in development called *anhidrotic ectodermal dysplasia,* associated in this particular case with mental deficiency. In the majority of cases reported in the literature this condition, characterized chiefly by absence of sweat glands, a scarcity of hair growth on the scalp and in the axillary and pubic regions, and the presence of partial or total adentia, was accompanied by somewhat lowered mentality. Here is an ectodermal abnormality with a depressing effect upon the intellect—perhaps not so serious as in the conditions discussed above, but nevertheless a significant one. A gene frequency analysis[10] disclosed that there is good evidence to substantiate an earlier hypothesis, based upon studies of family pedigrees, that the condition is inherited as a sex-linked recessive. It is passed on through the daughters of affected males to half of the grandsons.

Conclusions

From what has been said it is evident that a start has been made in breaking down the conglomerate mass of conditions, known today as mental deficiency, into component clinical entities with definite pathology. Genetics may play an important role in this process.

5. Penrose, L. S.: Peripheral Nerve Tumours in Case of Phenylketonuria, Lancet 1:572 (March 11) 1939.
6. Ellis, R. W. B., Sheldon, W., and Capon, N. B.: Gargoylism, Quart. J. Med. 5:119 (Jan.) 1936.
7. Ashby, W. R., Stewart, R. M., and Watkin, J. H.: Chondo-osteo-dystrophy of Hurler Type, Pathological Study, Brain 60:149 (June) 1937
8. Kressler, R. J. and Aegerter, E. E.: Hurler's Syndrome (Gargoylism), J. Pediat. 12:579 (May) 1938.
9. Halperin, S. L. and Curtis, G. M.: The Genetics of Gargoylism, Am. J. Ment. Deficiency, 46:298 (Jan.) 1942.
10. Halperin, S. L. and Curtis, G. M.: Anhidrotic Ectodermal Dysplasia Associated with Mental Deficiency, In Press.

Where poverty, bad housing, overcrowding, malnutrition and other bad environmental factors coexist, as in Cyprus, tuberculosis need not assume serious proportions so long as massive infection is controlled. Per contra, experience at Saranac and Preston Hall shows that in communities where large numbers of open cases are congregated, but where there is no poverty, no bad housing, no overcrowding, no malnutrition—but where close watch is kept on families as a whole—healthy individuals nearly all escape.

The lesson is this: Infection and environment must be considered together and not separately as we have been wont to do. Infection itself is an environmental factor. Germs may lurk in dark, damp places but the darkest and dampest is the cavity in the lung which remains uncontrolled or uncollapsed, and all the public health measures in the world will not sanitate these, the most important source of infection Infection being present, other environment factors must be brought up to a specified standard if massive infection is to be avoided. In Britain now . . . let us search out the sources of infection, many of them unknown, and eradicate them, not waiting for the interplay of other environmental factors which sooner or later will lead to the spread of disease. Editorial. Lancet, Jan. 24, 1942.

Employ your time improving yourself by other men's documents: So shall you come easily by what others have labored hard for.—Socrates.

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JULY, 1942

THE ATLANTIC CITY SESSION OF THE AMERICAN MEDICAL ASSOCIATION

Those who attended the ninety-third annual session of the American Medical Association did not need to be reminded that our country is at war. As soon as a guest was ushered into a hotel room his eye was caught by the largest notice on the door, giving elaborate directions for conduct during an air raid. Under the glass cover of the dresser was another notice, which read: "We have been notified by the Federal Government to instruct all our guests, that between the hours of *Sundown* and *Sunrise*, whenever *Lights* are needed in Guest Rooms and Bath Rooms, that Shades Must be Drawn. This is a Temporary Order to test a satisfactory *Dimout*. The Management." (Capitals and italics the Management's.) The usually glaring boardwalk was so dimmed that it was difficult to distinguish faces only a few feet away. The row of lights, along the ocean front were painted black except for an oval slit on the boardwalk side. The shops and places of amusement that were open had shades drawn, with the word "Open" just visible to the passerby.

Much of the scientific program and many of the scientific exhibits were given over to military medicine. The addresses of the officers, and much of the business of the House of Delegates, dealt with the part the medical profession must play in the war. The chief speaker at the annual banquet of the Delegates and Officers, Mr. Paul McNutt, dealt none too gently with the urgent need for doctors.

In spite of the war, gasoline rationing, and the real hazard created by the target such a gathering offered to one of Hitler's submarines, the registration reached the gratifying mark of 8,238. North Carolina was well represented, with 96 registered. Only twelve other states had more in attendance. She was also well represented on the scientific program, with three presenting papers before section meetings, five discussing papers, and three taking part in scientific exhibits. North Carolina's own son, Fred Rankin, was installed as President at the opening General Session. His presidential address was excellent.

The Scientific Exhibit justified its reputation as the greatest postgraduate course in the world. The general scientific meetings and the programs of the section meetings attracted large numbers.

Our South American visitors appeared to enjoy every minute of the meeting, and entered into the various programs with gusto. It is to be hoped that the good neighbor policy of this meeting will be continued in the future.

The proceedings of the House of Delegates will be published in detail in the *Journal of the A.M.A.* The unanimous selection of Dr. James E. Paullin, distinguished internist of Atlanta, as President-Elect, met with general approbation, as did the selection of William J. Carrington of Atlantic City as Vice President. Dr. Carrington seems to be the perpetual chairman of the Committee on Arrangements for the Atlantic City sessions of the A.M.A. He is a member of the National Physicians' Committee, and one of the most popular members of the Association. The two speakers before the House of Delegates who perhaps were given the most applause were Dr. T. C. Routley, who represented the Canadian Medical Association, and Dr. Benvenuto R. Dino, of the Philippines. Both men spoke briefly but most effectively.

The Ninety-Third Annual Session was, in the words of an editorial in the *Journal of the A.M.A.* for June 20, "a triumph in its accomplishments, a tribute to the indomitable spirit of American Medicine."

MEDICAL EDUCATION AND THE WAR

Forty years ago there were one hundred and sixty-six medical schools in the United States, more than one hundred of which were infamous diploma mills which almost irreparably damaged the medical profession by filling it with incompetent men. The famous Flexner report of 1910 upon medical education decimated the dreadful schools, and kindly nature has gradually removed their product from the medical scene. During the past three decades the quality of medical education has steadily improved, until today one may say truthfully that in this type of education America leads the world.

The war has brought a new and subtle danger to medical education. Young graduates are denied more than one year of intern training, a restriction which is said to be a military necessity, and one, therefore, in which the profession gladly concurs, although recognizing it as a misfortune for the future of American medicine. Now, however, great pressure is being brought on the medical schools to strip their teaching staffs to the point where good medical training will become impossible, and this at a time when the schools have increased their enrollments materially, and are teaching continuously throughout the year.

This war will end, and, like all other wars, will influence very little the daily lives of the people.

"How little of all that human hearts endure

"Can kings or laws either cause or cure!"

Physicians will still be needed—good physicians—to help in the healing of the wounds of a sadly disillusioned world. In the hysteria which is inseparable from war, let us stand as a profession sufficiently aloof from the ever-mounting stream of suggestibility to insist that medicine be not subjected again to an influx of ill-trained and incompetent physicians. We must and will win the war, but unless clear judgment prevails, we may lose quite unnecessarily some of the irreplaceable needs of the peace that is to come.

NATIONAL PHYSICIANS' COMMITTEE APPROVED BY THE AMERICAN MEDICAL ASSOCIATION

Ever since the National Physicians' Committee for the Extension of Medical Care was created in 1939, the question of its relation to organized medicine, especially to the American Medical Association, has been repeatedly raised. Many have said that they would be willing to support it if they knew it had the full approval of the American Medical Association. At its recent meeting, the American Medical Association, through its House of Delegates, left no doubt of its approval of this Committee, by the adoption of the following resolutions:

WHEREAS, The physicians of the United States, through the American Medical Association, unselfishly have devoted time, energy and continuously greater ability to building an organizational structure truly nationwide in scope, serving every town, village and hamlet in this country and devoted to the vital task of providing a more effective and a more generally available medical service than is provided anywhere else in the world; and

WHEREAS, These efforts, over a period of nearly one hundred years, have developed American medicine to the point of a general recognition of its worldwide leadership; and

WHEREAS, This unparalleled growth and this unusual effectiveness are the results of the high level of educational requirements, the high standard of ethics that has been maintained and the continuous safeguarding of the relationship between the physician and the patient; and

WHEREAS,We are now passing through a period of worldwide revolutionary change in social, economic and philosophic concepts; and the general public has been and is subjected to a vast educational propaganda, some of which tends to discredit the American doctor and to destroy confidence in the effectiveness of American medicine and in our system of distributing medical care; and

WHEREAS, Preservation of the vital principles responsible for medicine's past progress, its present effectiveness and its ability to serve the public most advantageously make it essential that citizens understand the basic facts in connection with American medicine's methods, growth, achievements, the factors responsible for its superiority and the extent to which the people have been the beneficiaries of the profession's intensive and constructive efforts; therefore be it

Resolved, That we register our approval of the activities of the National Physicians' Committee for the Extension of Medical Service, commend the board of trustees and the management of that institution for the efforts they have made to enlighten the general public in connection with American medicine's methods, progress and achievements and in pointing out that the public has a vital interest in the final result; and be it further

Resolved, That it be declared the policy of this House of Delegates to encourage this effort and similar efforts with identical purposes.

IN DEFENSE OF MR. McNUTT

The after-dinner guest speaker of the House of Delegates on June 8 was the Honorable Paul V. McNutt. His subject was "The Urgent Need For Doctors." In this address he spoke very plainly, and his plain speaking has incurred some resentment. Before making up one's mind too quickly, however, one should read the address, which was given first place in the *Journal of the American Medical Association* for June 20. After a careful reading, whatever one's personal opinion of Mr. McNutt, it is hard not to admire his frankness in telling the representatives of organized medicine some unpleasant facts.

Mr. McNutt is not personally responsible for the fact that the army and navy are both desperately in need of doctors, in order to maintain the quota set by the powers that be. Neither is he responsible for the fact that, as Dr. Donnell Cobb points out in his President's Message this month, the medical profession will be expected to send one-third of its membership into service—a greater sacrifice than is demanded of any other group of men. Some months ago this JOURNAL ventured to suggest that the army was demanding a disproportionately large number of medical men as compared with the civilian population. No lack of patriotism was intended then, nor is it intended now, in raising the question again. The depletion of our ranks by one-third—and these the most able-bodied—will still further increase the gap between the civilian-physician and the soldier-physician ratios.

It is true that many doctors have been confused by the forms sent out from Colonel Seeley's office, and thought that they were applications for commissions. Certainly the impression was conveyed that filling them out and indicating one's preferences for service was equivalent to volunteering. When it is remembered that more than 130,000 of these forms have been returned to Colonel Seeley's office, and that this number represents roughly three fourths of the doctors in the United States, it seems unfair to term the medical profession slackers.

What was worrying Mr. McNutt was that these tentative offers to volunteer had not been followed up by enough signatures on the dotted lines of real application blanks. He can hardly be blamed for looking at the record as it actually is, and noting that the army and navy are short of the actual number of doctors they need to fill out the quota. Very shortly letters will be sent out over Dr. Frank Lahey's signature to those doctors who signified their willingness to serve, who are suitable for service, and who have not yet joined the army or navy, urging that they apply at once for commissions.

The medical profession is the only group entrusted by the government with the responsibility of selecting its quota for military service. It is a tremendous order to send one third of our number—two thirds of those under 45—to the army and navy. It will mean adding 50 per cent to the load of every man left at home. Nevertheless, Mr. McNutt need not fear that the medical profession will betray its trust. Let us hope that neither he nor other officials of the Administration will forget two promises made the House of Delegates at Atlantic City. The first was that "'All out' collaboration does not involve any theoretical assaults on, or support of, any theory of medical practice." The second promise was that if organized medicine does its duty in obtaining enough physicians for the army and navy, and at the same time allocates men to important positions in industry and in civilian life, "the profession should certainly have no fear of any drastic change in medical practice after the war."

* * * *

NORTH CAROLINA'S QUOTA REACHED

Just as the NORTH CAROLINA MEDICAL JOURNAL was ready to go to press, an important communication was received from Dr. Hubert Haywood, State Chairman of Procurement and Assignment of Physicians. General Coburn has just returned from Washington with the gratifying news that North Carolina is one of the first states in the Union to reach its 1942 quota of doctors for military and naval service. While anyone who feels the urge to volunteer may still do so, it is probable that Uncle Sam will not demand any more medical officers from North Carolina this year.

Much praise is due Dr. Haywood and his committee, as well as those medical men who have voluntarily left their practice and gone to the defense of the country.

CASE REPORTS

CLINICO-PATHOLOGICAL CONFERENCE

CITY MEMORIAL HOSPITAL WINSTON-SALEM

Presentation of Case

E. B., a 56 year old Negro woman, was admitted to the Kate Bitting Reynolds Memorial Hospital February 26, 1942, because of marked anasarca. Her chief complaint was "swelling all over".

Her present illness began gradually in August, 1941, when she noted swelling of her ankles which gradually progressed and extended upward. Her abdomen finally became swollen and her urinary output decreased. She also noticed progressive dyspnea. She was seen by the City Physician in November, at which time marked edema was noted on the dependent side, arm, leg and face, while the upper side was almost free of swelling. Urinalysis at that time showed a 4 plus reaction for albumin, but no formed elements. Treatment with ammonium chloride produced satisfactory diuresis and loss of edema. She was later given 3 cc. of mercupurin with even more improvement. She was then able to get out of bed for the first time in over a month. However, edema eventually progressed to a maximum extent, and the patient was orthopneic and bedridden when she was finally admitted to the hospital. There was no family history of heart or kidney disease, and no diabetes or other familial disorders. The parents died of unknown causes. The patient recalled having had only the childhood diseases and malaria. She had been in good health prior to her present illness. There was no history of venereal disease.

The physical examination, on admission, revealed a middle aged woman in moderate orthopnea, bloated with massive anasarca. Examination of the head, eyes, ears, nose and throat was essentially negative. The chest revealed signs of "some fluid in the bases". The heart was slightly enlarged to the left. There were no murmurs or arrhythmia. The abdominal examination elicited signs of ascites, and the liver edge was palpable.

The urinalysis on admission showed a specific gravity of 1.027 with 9 to 11 white blood cells, occasional red blood cells, and 10 granular casts per high power field. The blood studies were omitted because of technical difficulties resultant from the massive edema.

Her course in the hospital was steadily downhill, and death occurred on the eighth hospital day. Treatment consisted of diuretin, ammonium chloride, 50 cc. of 50 per cent glucose, mercupurin 2.2 cc., digitalis, and hot packs. Fluids were limited; the output, however, remained lower than the intake. The urinalysis two days before death gave essentially the same findings as the previous one, except that hyalin, waxy and fatty casts were reported.

Discussion

DR. O. E. WRIGHT: The first thing that the average doctor would think of when he sees a patient orthopneic and edematous throughout is congestive heart failure. Of course, there are other conditions that cause generalized dropsy—among them, renal insufficiency, pressure from tumors, anemias, and constrictive pericarditis. This woman complained of "swelling all over". In November, 1941, her urine gave a 4 plus reaction for albumin. That points toward a kidney damage at that stage. She was given diuretin and the edema subsided to a great extent. Later it recurred, and ascites developed. The ascites alone could be caused by an obstruction to the portal circulation or by tumor pressure in the abdominal cavity. With a portal obstruction alone you would not get a generalized edema, however, and that was the symptom which was stressed when she first came in. The fact that she steadily grew worse and died in eight days leads me to believe that she had severe congestive heart failure associated with renal insufficiency. The two conditions are often seen together. With renal insufficiency there is increased blood pressure and cardiac failure in the end. I notice that the systolic pressure was down to 130 after her admission to the hospital, and I am assuming that an acute dilatation of the left ventricle had occurred, accounting for the systolic pressure drop. My diagnosis is chronic glomerular and tubular nephritis, producing the typical nephrotic syndrome, high albuminuria and massive edema with resulting circulatory failure. Cirrhosis of the liver probably accounts for some of the ascites.

Clinical Diagnosis

Nephrosis.

Dr. Wright's Diagnosis

Congestive heart failure resulting from glomerulo-tubular nephritis.

Gross Anatomical Diagnosis

Subacute glomerulo-nephritis.
Anasarca.
Pulmonary edema.
Hemorrhagic erosion of the gastric mucosa.
Infarct of the right kidney.
Myocardial infarction.
Intussusception of the small intestine.
Scar of the right thigh.

Pathological Findings

DR. T. T. FROST: The patient was tremendously water logged. Most of the fluid was in the tissues and there was not so much in the serous cavities. The heart was of normal size, weighing 275 Gm., and it showed a few small, fairly average, myocardial scars over the left ventricle, the largest probably 1 cm. in diameter and extending for a distance of 3 or 4 mm. into the muscle. The lungs were heavy and a dull purple-red in color, and there were a few areas of consolidation. The liver was somewhat enlarged, weighing 1075 Gm., and was somewhat pale from the cloudy swelling which was present. Hemorrhagic erosions were found in the stomach, and there was hyperplasia of the lymphoid tissue in the duodenum. The small intestine contained an intussusception which had evidently been present for a long time, because it could not be reduced. The intussuscipiens and intussusception were joined by fibrous adhesions. It was a chronic intussusception without any obstruction. There was no dilatation of the bowel above it.

The kidneys were a little bit larger than normal, weighing 400 Gm. together. In the right kidney there was an infarction which was due to a thrombus of one of the arteries. The kidneys had a smooth surface and were quite pale. Small cysts were also visible. The cortex was a little bit wider than normal. There was nothing suggestive of chronic glomerular nephritis except the small cysts. The section of kidney near the pelvis showed the tip of a papilla projecting into one of the calyces. There was marked dilatation of all the tubules, and the tubular epithelium had disappeared. A small amount of inflammatory reaction was present. There were granular debris and casts in the tubules, and the glomeruli showed changes of subacute glomerular nephritis, fibrosis of the capsule, and fibrosis of the tufts with adhesions of the tufts to the capsule. In one glomerulus the tufts were markedly lobulated, thickened and adherent at one point to the capsule. The arterioles in the other kidney appeared normal. There was no thickening. Two of the glomeruli showed the changes of a subacute intracapillary glomerular nephritis, with increased cellulation, fibrosis of the tufts and adhesions to the capsule of Bowman. The aniline blue stain accentuated the fibrosis of the glomerular tufts and brought out hyalin casts in the tubules.

This woman had a mild subacute glomerular nephritis of the nephrotic type. The most outstanding change appearing through all the sections of the kidney was the increased atrophy of the tubular epithelium. The lungs showed edema and very little passive congestion. The heart showed a minor degree of myocardial fibrosis, a small area of fibrosis representing a healing infarct.

Intolerance to Diethylstilbestrol

Nausea and vomiting have been the most frequent side-effects following administration of Stilbestrol (diethylstilbestrol). A recent report (J. A. M. A., 119:400, May 30, 1942) points out that there is a definite relation between these symptoms and the nausea and vomiting of early pregnancy. If one will merely take the time to ask the prospective patient if she had nausea and vomiting with a previous pregnancy, it would serve as a warning to give not over 0.25 mg. daily as an initial dose. Desensitization may be accomplished by giving 0.1 mg. tablets once daily for five days, then increasing the dose gradually until the therapeutic level is reached. Diethystilbestrol, Lilly (formerly known as Stilbestrol) is available in 0.1 mg. tablets, as well as in larger doses, for oral administration.

Summer Diarrhea in Babies

Casec (calcium caseinate), which is almost wholly a combination of protein and calcium, offers a quickly effective method of treating all types of diarrhea, both in bottle-fed and breast-fed infants. For the former, the carbohydrate is temporarily omitted from the 24-hour formula and replaced with 8 level tablespoonfuls of Casec. Within a day or two the diarrhea will usually be arrested, and carbohydrate in the form of Dextri-Maltose may safely be added to the formula and the Casec gradually eliminated. Three to six teaspoonfuls of a thin paste of Casec and water, given before each nursing, is well indicated for loose stools in breast-fed babies.

Please send for samples to Mead, Johnson & Company, Evansville, Indiana.

MEDICOLEGAL ABSTRACT

J. F. Owen, M. D., LL. B.
Raleigh

Drunkenness. When a person is too drunk to be capable of entertaining a premeditated design or deliberate premeditation to kill he is not guilty of murder in the first degree unless he entertained such intent when he drank.

Frequently doctors are called upon to appear as witnesses to help determine a defendant's capability to entertain criminal intent. The following case was selected in order to show the effect of intoxication as it relates to those charged with first degree murder. Ordinarily, of course, voluntary drunkenness or intoxication is not an excuse for crimes, but there are exceptions to this rule, and this case represents one which is fairly common. It should be noticed, however, in this particular instance that while the degree of the crime might be lessened by the fact that the accused was intoxicated at the time the crime was committed, he was not wholly absolved from blame.

The defendant was convicted in Superior Court of murder in the first degree, and appealed to the Supreme Court from a death sentence. The main exception was as follows: "The court failed to charge the jury that a person who commits a murder when so drunk as to be incapable of forming a deliberate and premeditated design to kill would not be guilty of murder in the first degre but murder in the second degree or a lesser degree of homicide."

By way of explanation it perhaps should be stated in this connection, that murder in the first degree is the killing of a human being willfully, deliberately, and with premeditation, or a homicide committed in the perpetration or attempt to perpetrate any arson, rape, robbery, burglary, or other felony.

The defendant's testimony was to the effect that he and the deceased, who were at the time of the alleged homicide roommates and bed fellows, bought a half gallon of whiskey on the afternoon of Friday, August 7, 1937, and that they went to their room about 10 or 10:30 o'clock that night, after having drunk some of the whiskey; that they drank more whiskey after reaching the room, and that he remembers nothing more that happened that night. His testimony is further to the effect that when he awoke early on the morning of August 8, he found his roommate beside him in bed, dead, with his head bloody; that he removed the body to another place in the room and left later in the day, because he feared that he would be suspected of the homicide; that he did not remember or have any knowledge whatsoever of how the deceased came to his death; that he did not know whether he shot or killed the deceased; and that he did not plan or intend to kill the deceased.

The Judge of the Superior Court charged the jury to the effect that if the defendant formed a fixed design to kill and then got drunk and executed such intent while in a drunken condition, he would be guilty of murder in the first degree. When the case came before the Supreme Court the Justice stated that while the instruction of the court was correct as far as it went, it was error for the court even in the absence of a request to fail to charge the jury that if the defendant did not form any previous design to kill, and killed while in such a drunken condition that he was incapable of premeditation and deliberation, he would not be guilty of murder in the first degree. There was some suggestion by the State that the homicide was committed in the perpetration of a robbery and that the defendant was therefore guilty of murder in the first degree on this account, but the Supreme Court could see no proof that the crime was committed in perpetration or attempt to perpetrate a robbery. According to the record, there was no eye witness, and there was nothing in the alleged confession of the accused which related to robbery.

As was indicated above, error was found in the Judge's charge to the jury, and the case was returned to the Superior Court for a new trial.

(North Carolina Supreme Court, v. 217, p. 445. Decision rendered spring term, 1940.)

MILITARY MEDICINE

OFFICE OF CIVILIAN DEFENSE

Dr. Rankin Retires From Medical Advisory Board, OCD

Dr. Fred W. Rankin, Lexington, Kentucky, retired as a member of the Medical Advisory Board of the Office of Civilian Defense upon being called to active service in the Office of the Surgeon General of the Army. Dr. John T. O'Rourke, dean of the University of Louisville School of Dentistry, Louisville, Kentucky, has been designated to fill the vacancy on the Board.

Three important agencies—the Federal Security Agency, the Office of Civilian Defense, and the American Red Cross—have agreed upon plans to assist civilian victims of enemy action, in case of bombing.

Immediate responsibility for the care of persons injured as a result of enemy action is placed upon the Emergency Medical Service of the U. S. Citizen's Defense Corps. The Red Cross will assist in furnishing nurses aides, stretcher teams, ambulances, and supplementary equipment; it will not duplicate the work of the Emergency Medical Service.

Appointment of a Nurse Deputy to the Chief of Emergency Medical Service

In accordance with the recommendations contained in Medical Division Bulletin No. 1, the Medical Advisory Board of the local Emergency Medical Service includes a representative of the local nursing profession. Since this bulletin was issued, State and local nursing councils which include all nursing groups have been organized to provide for total nursing needs. Experience indicates that some one person must be assigned the responsibility for recruiting nurses for active duty with the Emergency Medical Service. Each State and local Chief of Emergency Medical Service should be urged to appoint a Nurse Deputy, and in selecting her he should consult the State or local nursing council. The Nurse Deputy must have organizing ability and be able to devote the time necessary for her important duties. If a nurse has been successfully carrying out the duties of a Nurse Deputy under some other title, a new appointment is not indicated.

The duties of the State Nurse Deputy are:

1. To assist the State Chief of Emergency Medical Service and the local Nurse Deputies in the State in mobilizing all members of the nursing profession for duty in the Emergency Medical Service during and after an enemy attack or other wartime disaster.

2. To aid the American Red Cross and the hospitals to carry through a full program of training of Nurses' Aides so that the depleted ranks of hospitals and public health nursing services may be assisted in carrying the heavy burden of wartime service in civilian hospitals and health departments, as well as in the casualty stations and first aid posts of the Emergency Medical Service.

3. To assist the State hospital officer and State Chief of Emergency Medical Service in the emergency assignment of private duty nurses, and of nurses from local and State hospitals and health agencies to base hospitals, if the need arises for the evacuation of patients from Casualty Receiving Hospitals of the coastal cities.

The duties of the local Nurse Deputy are:

1. To maintain an active file of available nurses, kept up to date by, at least, a monthly check-up. A copy of the complete file should be provided by the Nurse Deputy for the Chief of Emergency Medical Service. Duplicate cards should be on file at registries, hospitals or other suitable places for use in different parts of the community so that nurses may be secured for emergency duty in hospitals and casualty stations on short notice. In a large city, it is desirable to subdivide the duplicate file according to the districts or precincts in which nurses reside or work. In smaller towns or in rural distiicts only one file will be required.

2. In collaboration with the American Red Cross and the local Chief of Emergency Medical Service, to provide all nurses with a first aid course and instruction on gas protection and the care of chemical casualties.

3. To arrange with local agencies employing public health nurses, for home visits to (a) casualties slightly injured who have been allowed to return home without hospitalization; (b) convalescent patients discharged early from hospitals to make room for casualties; and to assist the local Chief of Emergency Medical Service to arrange for centralized reporting of the need for this nursing care in homes.

4. To assist the local chapter of the American Red Cross and the local hospitals to carry through a full program of training of Nurses' Aides for wartime service in civilian hospitals and health departments as well as in the casualty stations and first aid posts of the Emergency Medical Service.

This information should be transmitted to State Defense Councils and State Chiefs of Emergency Medical Service.

Decontamination of Eyes After Exposure to Lewisite

Reference is made to a news release under date of March 31, 1942, regarding the treatment of Lewisite burns of the eyes with hydrogen peroxide. Further carefully controlled work conducted by the National Research Council indicates hydrogen peroxide is entirely ineffective for treatment. Washing with large amounts of 2 per cent solution of sodium bicarbonate in water or with plain water is the most effective treatment and should be carried out as soon as possible after exposure.

This information should be transmitted to State Defense Councils and State Chiefs of Emergency Medical Service.

BULLETIN BOARD

PRESIDENT'S MESSAGE

As the War continues to go "not so well" for the Allied Nations, the responsibility and the duty of the medical profession seem to grow greater and to be brought into sharper focus.

The demand for doctors in the armed forces is great. Each new proposal for our army places it at a higher figure. An army of nine million will take approximately 6 per cent of our population. According to the present doctor-soldier ratio, it is estimated that one-third of all physicians (two-thirds under 45 years) will be needed for such an army. To take approximately 6 per cent of the general population for the armed forces and approximately 33 1/3 per cent of the doctors will greatly alter the proportion of doctors in civil life. Undoubtedly this will bring about hardships and will call for many readjustments.

Newspapers and periodicals are frequently calling attention to the approaching dearth of doctors in such a way as to instill fear and apprehension in the minds of the people, lest they find themselves unable to secure medical service in case of an emergency. Some county Procurement and Assignment committees are letting it be known publicly and in no uncertain terms that if they supply the number of physicians called for by their quota the remaining physicians will be utterly helpless in caring for the health of the community.

Let us bear in mind that the Procurement and Assignment Service was established at our own suggestion; that it is staffed by physicians and guided by physicians, and that ours is the only profession that has been given the opportunity to ration itself. Such a service should afford the fairest and most efficient means of dealing with this most complex matter. If we cannot perform this service for our country, for our patients, and for ourselves in a satisfactory manner, could other less interested persons do it better?

Let us bear in mind also that it may not be wise to frighten the civil population unnecessarily over the possible shortage of medical care. Dr. Griffith, in his President's Address, gave us some excellent suggestions as to ways in which our service can be used more efficiently. Unquestionably in the past

we have all too frequently squandered our services and our patients have, at times, used our services with a wasteful luxuriousness. Some county societies have already taken steps to organize better the services of the physicians remaining at home and to instruct the public how to utilize their services to a greater advantage and with greater economy.

By such means it is likely that all will have the necessary medical attention. To become unduly and prematurely concerned ourselves will only alarm our patients.

As a profession our first duty is to lend our every effort towards winning the War. Our second duty is to see that our people at home receive every possible medical care. Our third duty is to see to it that the physicians who are called into service can return to the same unhampered system of practice which they left.

There are now 8,000 alien physicians in the United States. North Carolina has always wished to be cared for by its own American doctors. Let us so organize ourselves and our work that we can continue to serve our people in the way they wish to be served. This is entirely the duty of each county society. It is earnestly hoped that we can discharge this duty in such a way that it will not be necessary to permit an influx of physicians who are alien to our country, to our state, to our way of life, and to our ideals and customs.

SECRETARY'S MESSAGE

July 20 is the dead-line!

We are aiming at the sky even if we hit a stump!

We are out to collect all dues for 1942. The following letter has been sent to each member whose dues have not been paid:

Dear Doctor:

Because we have no record of your 1942 dues having been paid, this reminder is sent with the suggestion that you send us your dues—$8.00—through your County Secretary, *if you are in an organized county,* or direct, *if you are not,* so that your name may be included on the Roster of Fellows for 1942 which will appear in the August issue of the NORTH CAROLINA MEDICAL JOURNAL. All material for this issue of the JOURNAL must be in the hands of the printers *early* in July. I, therefore, urge you to attend to this matter at once. Looking forward to the pleasure of placing your name on the Roster of Fellows for 1942, I am

Very truly yours,
(Signed)
Roscoe D. McMillan, M. D.

We are making an earnest effort to give every member an opportunity to pay his dues in order that his name may be on the Roster of Fellows which will appear in the August issue of the JOURNAL, along with the Transactions of the Charlotte meeting. The names of all members whose dues have not been paid by July 20 will be dropped from the JOURNAL mailing list. Of course, the August issue, giving the Proceedings of the 89th Annual Session, will be the most important issue of the year and I feel that no fellow who is interested in organized medicine in North Carolina will want to miss it.

The House of Delegates in Charlotte last month made a ruling that all members who are serving in the armed forces of the country will be exempt from payment of dues for the duration; any dues which have already been paid by men in service will be remitted. I have asked each county secretary to keep me informed throughout the year as their members leave for service. I regret that only a few have responded to my request. County Secretaries, please take notice! This is the only means I have of being officially notified as to the members who are serving with the armed forces and whose dues should be waived or remitted. The officers who attended the Presidents' and Secretaries' Breakfast in Charlotte have responded well. I am depending on each of you to keep me fully informed as your members leave to serve their country.

Remember—there are only a few days left to pay your dues.

For convenience and quick service, my address is:

Red Springs, N. C.
Box 232

In response to an inquiry to the State Department of Revenue regarding exemption from payment of State License Tax for doctors in military service, I have received a letter, from which I quote:

"I regret to advise that this matter has been discussed with the Attorney General and he advises that, under the law, there is no provision whereby relief may be

given. Persons continuing to practice their profession on and after June 1, are liable for the license tax levied under Section 109, of the Revenue Act.

"We are in sympathy with this cause and it is expected that the 1943 General Assembly will make some concession."

ROSCOE D. MCMILLAN, M. D.
Secretary-Treasurer

NEWS NOTES FROM THE BOWMAN GRAY SCHOOL OF MEDICINE OF WAKE FOREST COLLEGE

The Bowman Gray School of Medicine began its second term on June 29, with 119 students registering. There are 50 students enrolled in the first year class, 36 in the second year class, and 33 in the third year class. Instruction in the third year of medicine is being offered for the first time.

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At the meeting of the student body on June 29, announcement was made of the establishment of a $500 fund for visiting lecturers to be known as the Nathalie Gray Bernard Lectureship. This lectureship will be established through voluntary contributions of the students and faculty, and the fund will be set aside for the purpose of bringing to the school each year a nationally-known lecturer in the field of science or medicine.

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Dr. William A. Wolff begins his duties as Associate Professor of Biochemistry in charge of Chemical Pathology on July 1.

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Dr. Robert B. Lawson has joined the medical staff of the Bowman Gray School of Medicine as Assistant Professor of Pediatrics, and has opened an office for the private practice of pediatrics in the Private Diagnostic Clinic of the North Carolina Baptist Hospital. For the past two years, Dr. Lawson has been pediatric consultant to the State Health Department engaged in the teaching of refresher courses in pediatrics at Duke Hospital.

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Dr. Wingate M. Johnson, Professor of Clinical Medicine, was Secretary of the newly created Section on General Practice of the American Medical Association, which held its first sessions at the Atlantic City meeting.

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Dr. Tinsley R. Harrison, Professor of Medicine, gave a paper on "Some Puzzling Aspects of Pain in the Chest" before the Section on General Practice of the American Medical Association. Dr. George T. Harrell, Associate Professor of Medicine, discussed a paper before the Section on Dermatology and Syphilology.

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Dr. Howard H. Bradshaw, Professor of Surgery, spoke at Class Reunion Day at Jefferson Medical College on June 3. His subject was "Surgical Aspects of Carcinoma of the Cardiac End of the Stomach".

NEWS NOTES FROM THE UNIVERSITY OF NORTH CAROLINA

The Josiah Macy, Jr. Foundation has renewed its grant to the Department of Pharmacology in continued support of Dr. W. deB. MacNider's study of the Ageing Process.

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Under the accelerated program for medical education the Medical School opened its session for 1942-43 on June 15 with a total enrollment of ninety-one students. Forty-two are in the second year class and forty-nine in the first year class.

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Mr. J. Reece Blair, formerly an instructor in Physiology and Biological Chemistry at the Alabama School of Medicine, has been appointed instructor in Physiology to replace partially Dr. H. D. Bruner, on leave of absence in government service.

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The Department of Public Health Nursing, the newest development in the School of Public Health at the University of North Carolina, has recently received national recognition by being accredited by the National Organization for Public Health Nursing. It is now one of the twenty-seven approved programs of study in public health nursing for graduate nurses in universities throughout the United States and is therefore in the top rank of professional education for the expanding field of public health.

During the first year fifty-seven graduate nurses have been enrolled, and at Commencement seventeen received Certificates in Public Health Nursing and three the Bachelor of Science degree in Public Health Nursing.

NEWS NOTES FROM THE STATE BOARD OF HEALTH

Our vital statistics in general have been extremely gratifying during this first year of our actual participation in hostilities. So far there have been 12,792 deaths in North Carolina in 1942, which is 1,632 fewer than occurred during the first five months of 1941.

NEWS NOTES FROM THE NORTH CAROLINA TUBERCULOSIS ASSOCIATION

Walter S. Page, Jr., State Field Worker, resigned his position with the North Carolina Tuberculosis Association on May 15 and will volunteer his services to the Armed Forces.

The following persons from North Carolina attended the Annual Meeting of the National Tuberculosis Association in Philadelphia:

Dr. P. P. McCain, Sanatorium
Dr. Paul Ringer, Asheville
Dr. A. L. Ormond, Black Mountain
Dr. H. L. Seay, Huntersville
Dr. David T. Smith, Duke University
Dr. M. D. Bonner, Jamestown
Dr. R. L. Carlton, Winston-Salem
Frank W. Webster, Raleigh

The theme of this year's meeting was—"Tuberculosis Work in a World at War". Dr. J. Burns Amerson, Jr., of New York City, was elected president of the National Tuberculosis Association and Dr. Lewis J. Moorman of Oklahoma City, President-elect. Dr. Henry C. Sweany of Chicago was made president of the American Trudeau Society and Arthur J. Strawson of Boston was elected the president of the National Conference of Tuberculosis Secretaries. Mrs. Ashley Halsey of Charleston, S. C. was made Vice President of this group.

Alamance-Caswell Counties Medical Society

The Alamance-Caswell Counties Medical Society met on June 9 and elected a new President and Vice President for the remainder of the year. Dr. W. W. Tyson, former President, is now in military service, and Dr. W. E. Cooke, former Vice President, has developed tuberculosis and has had to give up his practice. Dr. F. T. Harper of Graham was elected President, and Dr. J. B. Walker of Burlington Vice President.

Mr. Alvis Rich, local undertaker, showed two movie films: "Autopsy Technique" and "Autopsy Embalming Technique".

Buncombe County Medical Society

The Buncombe County Medical Society held its first dinner meeting of the year on June 22 at the S. and W. Cafeteria. Members of the medical faculty of the University of Georgia were guest speakers. Dr. Richard Torpin, Professor of Obstetrics and Gynecology, spoke on "Roentgenpelvimetry in Labor"; Dr. Robert B. Greenblatt, Professor of Experimental Medicine, spoke on "Pellet Implantation in Endocrine Disorders"; and Dr. Perry P. Volpitto, Professor of Anesthesia, gave a talk on the "General Use of Barbiturates".

Davidson County Medical Society

The Davidson County Medical Society held its regular dinner meeting at the Municipal Country Club in Lexington on June 3. Reports were given by the delegates to the State Convention and by the President and Secretary of the Society. Dr. Coy C. Carpenter, Dean of the Bowman Gray School of Medicine of Wake Forest College, discussed "Medical Education".

Forsyth County Medical Society

The Forsyth County Medical Society met at the City Memorial Hospital in Winston-Salem on June 9. Dr. L. A. Andrew, Jr., and Dr. C. N. Adams discussed "Male and Female Sterility".

Guilford County Medical Society

The Guilford County Medical Society held its regular monthly meeting in Greensboro at the O'Henry Hotel on June 4. The guest speaker was Dr. Henry P. Wagener of the Section on Ophthalmology of the Mayo Clinic. His topic was "Ophthalmoscopy as an Aid to General Medical Diagnosis".

Polk County Medical Society

The Polk County Medical Society met in Troy at St. Luke's Hospital on June 9. Dr. M. C. Palmer, delegate to the State Medical Society, reported on the Charlotte meeting, and the local situation was discussed. One of the five active members of the Society left for military service on June 15.

Southern Pediatric Seminar

The 22nd Annual Session of the Southern Pediatric Seminar will be held at Saluda, North Carolina, July 20 - August 1. Dr. Samuel F. Ravenel of Greensboro is Dean, Dr. Frank Howard Richardson of Black Mountain Vice-Dean, and Dr. D. L. Smith, Saluda, is Registrar. Dr. Oren Moore of Charlotte is Dean of Obstetrics, and the obstetrical division has been enlarged.

News Notes

North Carolina physicians appearing on the program of the Ninety-Third Annual Session of the American Medical Association, held in Atlantic City June 8-12, were Edwin P. Alyea of Durham, Tinsley R. Harrison of Winston-Salem, and Julian M. Ruffin of Durham, who presented papers before various section meetings; and Lenox D. Baker of Durham, J. Lamar Callaway of Durham, Worth B. Daniels of Fort Bragg, George T. Harrell of Winston-Salem, and Wingate M. Johnson of Winston-Salem, who were discussants of papers. Drs. Deryl Hart and Samuel E. Upchurch of Durham presented a scientific exhibit in the Section on Surgery, and Dr. Harry Winkler of Charlotte was one of the demonstrators who assisted in the special exhibit on fractures. Dr. Wingate M. Johnson of Winston-Salem was Secretary of the Section on General Practice.

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Among the doctors from North Carolina registered at the American Medical Association meeting in Atlantic City were the following:

Allen, Charles I., Wadesboro
Anderson, William Banks, Durham
Baker, Lenox D., Durham
Bass, H. Hartwell, Jr., Henderson
Bass, Spencer P., Tarboro
Bell, Orville E., Winton
Billings, G. M., Morganton
Bizzell, Thomas Malcolm, Goldsboro
Bradshaw, Howard Holt, Winston-Salem
Brockmann, H. L., High Point
Bulluck, Ernest S., Wilmington
Caldwell, Lawrence M., Newton
Callaway, J. Lamar, Durham
Carr, Eugene M., Asheville
Carrington, George L., Burlington
Carter, Frances Bayard, Durham
Christian, Thomas B., Raleigh
Clayton, Milton B., Statesville
Clement, Edward B., Salisbury
Cocke, C. H., Asheville
Combs, Fielding C., Winston-Salem
Cooke, Q. E., Murfreesboro
Cooley, Samuel S., Black Mountain
Crisp, Sellers M., Greenville
Dale, Grover C., Goldsboro
Daniels, Worth B., Fort Bragg
Davenport, Carlton A., Hertford
Davison, Wilburt C., Durham
Dees, Ralph E., Greensboro
Edwards, B. O., Asheville
Fearrington, J. C. Pass, Winston-Salem
Fike, Ralph L., Wilson
Franklin, Robert Benjamin, Clinton
Frizzelle, M. T., Ayden
Gold, Benjamin, Shelby
Graham, William A., Durham
Griffin, M. A., Asheville
Grouch, A. McR., Wilmington
Hackler, Robert Hardin, Jr., Washington
Hamblen, Edwin C., Durham
Harrell, George T., Winston-Salem
Harrison, Tinsley R., Winston-Salem
Hart, Deryl, Durham
Hicks, V. M., Raleigh
James, Arthur A., Jr., Sanford
Johnson, Walter R., Asheville
Johnson, Wingate M., Winston-Salem
Kelly, Luther W., Charlotte
Kendall, Ben H., Shelby

Lancaster, William J., Wilmington
Lane, Bessie Evans, Raleigh
Lapsley, A. Fraser, Badin
Leinbach, Robert Frederic, Charlotte
Lock, Frank R., Winston-Salem
McCutcheon, W. Benson, Durham
McElwee, Ross S., Statesville
McLeod, John P. U., Marshville
McMillan, Robert L., Winston-Salem
McNeill, James H., North Wilkesboro
McPherson, S. D., Durham
Massey, Charles C., Charlotte
Monk, H. L., Salisbury
Monroe, Lance T., Kannapolis
Noel, William W., Henderson
Norris, Francis L., Beulaville
Northcutt, Eugene E., Hatteras
Northington, James M., Charlotte
Outland, Robert B., Rich Square
Owens, Z. D., Elizabeth City
Padgett, Philip G., Kings Mountain
Persons, Elbert T., Durham
Phillips, E. N., North Wilkesboro
Rainey, William T., Fayetteville
Richie, Richard F., Raleigh
Robinson, John D., Wallace
Rude, Joe C., Durham
Sharpe, Frank A., Greensboro
Shaver, W. T., Albemarle
Sigman, F. G., Spencer
Sisk, Wilfred N., Asheville
Smith, David T., Durham
Spoon, S. C., Jr., Burlington
Sprunt, Douglas H., Durham
Tayloe, John C., Washington
Thacker, Edgar A., Goldsboro
Thomas, Wilbur Clyde, Winston-Salem
Tice, Walter T., High Point
Tuggle, Allan, Charlotte
Tuttle, Marler Slate, Kannapolis
Valk, A. de T., Winston-Salem
Walton, C. L., Glen Alpine
Westcott, William E., Asheville
Whitehead, Seba L., Asheville
Winkler, Harry, Charlotte

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Dr. C. H. Cocke of Asheville was elected Vice President of the American College of Physicians at its annual meeting, and was presented with a gavel in recognition of his services as Chairman of the Board of Governors from 1935 to 1942.

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Dr. Otto Billig of Asheville has been elected a member of the American Psychiatric Association.

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Dr. William St. J. Jervey of Tryon reported for active service in the United States Army on June 15.

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Dr. Roy Bunts of Asheville has received a commission in the Navy, and Dr. John Dougherty in the Army.

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Dr. D. H. Nisbet, who has recently moved from Charlotte to Atlantic Beach, is there for the summer only. He plans to resume practice in Charlotte in January.

AUXILIARY

A MESSAGE FROM THE PRESIDENT

With the advent of war and its attendant changes in the life of our nation comes a new perspective, a new philosophy, of service and sacrifice. Vacations are little spoken of, and busy minds and busy hands are learning to be prepared for constructive efforts in the multiple tasks that lie ahead.

We are aware that as women of this nation we must qualify ourselves to take our places where we are best fitted to serve. As the wives of doctors we have a definite commitment in the program of Medical Defense. Our husbands will be burdened with added responsibilities, and whatever demands are upon us, our first duty is to them and to the Medical Profession. We as an Auxiliary must incorporate into our program such projects as will be most effective in these times. It is both sobering and challenging to realize this obligation. In the mass of appeals that beset us every day for the use of our time and energy, let us resolve to discriminate carefully as to the ones that are most valuable.

Our national leaders of the Medical Auxiliary have worked out a formidable program for the State Auxiliaries. We are urged by our National President to become leaders in the community health program by:

1. Enlisting our services in the many branches of defense work;
2. Showing what scientific medicine is doing for public health and welfare;
3. Education against the danger of cults and charlatanism;
4. Education in the community control of the practice of medicine;
5. Educational crusades against falsely premised legislation;
6. Education to have all opinions emanate from the medical profession, which combines life-giving, and life-saving knowledge with unstinting labor. There is no rational control otherwise.

Is there a doctor's wife in North Carolina who would not give her best efforts to the furtherance of these ideals? It has been said, "Women know how to get things done." When there is something to be accomplished we know that leaders are needed. There are many such women, the wives of men of the Medical Profession, who are highly trained and well equipped to serve in capacities of

leadership, yet who are not members of our organization. Every element in the life of our Auxiliary can be gauged by the enthusiasm of its leaders. Enthusiasm can be taught and caught. May I urge that each member spread this enthusiasm throughout the coming year? We shall find many responsive souls, who will also catch the glint of fellowship and comradeship in working together.

In our program of varied activities we can find interests best suited to our ability. Every one among us is fitted to do some particular thing better than another. There is a place wating for each one of us. What will you do to make our Auxiliary stronger, our service greater?

Mrs. Sidney Smith, chairman of organization and immediate past president, is formulating plans with her ten councilors for expanded organization. Through her capable leadership of the past year, six new auxiliaries were added to our list, and we believe that this year will bring even greater results

Through instructive programs we shall gain information pertaining to Health Defense and other Auxiliary projects, both nationally and in the state. Much valuable information may be found in the following publications: *Hygeia*, the *Bulletin of the National Auxiliary, Handbook for the State Auxiliaries*, the editorial and auxiliary pages of the NORTH CAROLINA MEDICAL JOURNAL, the *Journal of the American Medical Association*, and the Transactions of the State and National Auxiliaries. The program chairman has compiled a list of speakers who have consented to address our Auxiliary on subjects of special interest.

Let us keep on the alert and acquaint the public with matters concerning medical legislation and public relations. It has been said, "Freedom of speech and freedom of the press is a privilege, but self-restraint is a virtue." Therefore let us be well informed on these matters so that we may be able, judiciously, to discuss them. In the various groups to which we belong we may be able, by an opportune word or impetus of thought in the right direction to mold a sentiment favorable to sound legislative enactments.

Our State Auxiliary philanthropies deserve our heartiest support. We shall endeavor to give our best efforts to the McCain Bed and Endowment Fund, the Stevens Bed Fund, and the Student Loan Fund. During the year we have been privileged through the McCain Bed Fund to care for three young women, who are now recovered and back in active service, and one young doctor who is very much improved. The Stevens Bed Fund took care of two patients, one a doctor and one a nurse, both of whom are now back on active duty; another nurse has recently been admitted. This June we were happy to have one of our Student Loan Fund boys graduate in engineering at State College, and another boy graduate in medicine at George Washington University.

Through our affiliation with the Southern Medical Auxiliary we shall continue our contributions to the Jane Todd Crawford Memorial Fund. Our State Research Chairman will compile information on an eminent North Carolinian of the Medical Profession, to be contributed to the Southern Medical Lending Library.

The Board of Directors of the Auxiliary has created a new state chairmanship to be known as "Doctors' Day." We hope that each County Auxiliary president will appoint a corresponding chairman in her respective unit. In this way we may work toward a larger and fuller program, honoring the doctors on National Doctors' Day, March 30.

It would be difficult to estimate the time and effort spent in the work of National Defense. Some of the Auxiliary and individual activities are Red Cross classes, Civilian Defense, contribution to the Medical and Surgical Relief Committees of America, assisting in the selling of Defense Stamps and Bonds, the establishment of blood and plasma banks, health defense through Cancer Control and Tuberculosis Campaigns. Let us continue to work with renewed zeal, wherever we find work to be done.

We cannot deny that these are troublous and momentous times for all of us. We live in a world seemingly bent on death. Yet the influence of the One who said, "I came that they might have life, and that they might have it more abundantly," is still abroad in our land. May we, the wives of doctors, the ministers of healing, exert our influence to keep this spirit alive.

MRS. R. A. MOORE,
President

BOOK REVIEWS

Methods of Treatment. By Logan Clendening, M. D., Clinical Professor of Medicine, University of Kansas; and Edward H. Hashinger, M. D., Clinical Professor of Medicine, University of Kansas, with chapters on special subjects by various authors. Ed. 7. 997 pages, 138 illustrations. Price, $10.00. St. Louis: The C. V. Mosby Company, 1941.

In this new edition Dr. Clendening has been joined by Dr. Hashinger as co-author, and by a group of his associates who have contributed chapters on special subjects. The new drugs which have won a place in medicine are included in this revision. This book is characterized by the pungent, clear style and virility of expression for which the senior author is noted. It is replete with interesting literary and historical comments. Although it is not encyclopedic in content, all the important methods of treatment used by the general practitioner are included. Physical methods of therapy and a discussion of psychotherapy are included, but the treatment of the latter is rather sketchy. The poorest section of the book, in the reviewer's opinion, are the chapters dealing with endocrine products. These are Chapter V, entitled "Extracts of the Ductless Glands", and Chapter XXII, on "Diseases of the Ductless Glands". The contents of these two chapters scarcely harmonize. For example, the use of salt and cortical extracts for Addison's disease are described in Chapter V but are ignored in Chapter XXII, where epinephrine, which in the reviewer's opinion is not only useless in this condition, but actually harmful, is described. The outmoded "Muirhead" treatment is still given space. In spite of these criticisms the book should prove both pleasant and instructive reading for the general practitioner.

Internal Medicine in Old Age. By Albert Mueller-Deham, Associate Visiting Physician, Welfare Hospital for Chronic Disease, Department of Hospitals, New York City; formerly Clinical Professor of Internal Medicine, University of Vienna Medical School, and Chief of Medical Division, Municipal Hospital for Chronic Disease, Vienna; and S. Milton Rabson, M.D., Assistant Professor of Pathology, New York Post-Graduate Medical School, Columbia University; Lt. Commander U. S. Naval Reserve. 395 pages. Price, $5.00. Baltimore: Williams and Wilkins Co., 1942.

The present volume is another in the series which have resulted from the recently increased interest in geriatrics, the study of old age. The book is a collaboration of a clinician of wide experience in the study of chronic disease in the aged with a pathologist interested in the abnormalities associated with senility. The book summarizes in a clear and lucid manner the intricacies of diagnosis and treatment of all the common and rarer disorders which are encountered in the aged. The complications induced in disease processes by the ravages of age frequently confuse the clinical picture as it presents itself to the physician. Because of its emphasis on these diagnostic features and complications as well as on the oft-times difficult problems of therapy, the present book can be read with profit by the general practitioner who is faced with an increasing proportion of old persons among his patients.

Clinical Parasitology. By David L. Belding, M. D., Professor of Bacteriology and Experimental Pathology, Boston University School of Medicine; Member of staff of Evans Memorial, Massachusetts Memorial Hospitals. 888 pages, illustrated. New York, London: D. Appleton-Century Company, 1942.

This excellent text has been written from the standpoint of the medical man rather than of the zoologist. Extensive use is made of diagrams to illustrate the relationship between the different parasitic forms, intermediate hosts, and the transmission to human beings. Excellent photographs of major pathologic changes in the diseases in human beings are included. Pathogenesis, diagnosis, prognosis and treatment are included for the more important diseases; special emphasis has been placed on prevention of parasitic diseases. Seventy pages of technical methods are included as a separate section. References are included after each chapter, and there is a general bibliography at the end. This subject should assume increasing importance in view of the anticipated increase in such diseases on the return of military forces from widely scattered parts of the globe; this volume will serve admirably to refresh recent graduates or to instruct older physicians who did not have the subject included in their curriculum.

Diseases of the Skin. By Frank Crozer Knowles, M. D., Assistant Professor of Dermatology, Jefferson Medical College; Edward F. Corson, M. D., Clinical Professor of Dermatology, Jefferson Medical College; and Henry B. Decker, M. D., Professor of Dermatology, Jefferson Medical College. Ed. 4, revised, with 272 illustrations. 621 pages. Price, $7.00. Philadelphia: Lea and Febiger, 1942.

The present volume is a revision of earlier editions by the senior author. It considers the conventional diseases encountered in dermatologic practice, with sections on synonyms, definition, symptoms, etiology, pathology, diagnosis, prognosis and treatment. The book is amply illustrated, but unfortunately it is difficult to portray adequately skin lesions by the ordinary black and white illustrations. The use of modern color photographs would have added greatly to the value of the book. In spite of this drawback the book will be of value for its clear, concise and orderly description of the skin lesions which the general practitioner is apt to encounter.

Bacteriology Laboratory Technique. By E. S. King, M. D., Professor of Bacteriology, Bowman Gray School of Medicine of Wake Forest College. 172 pages. Price, $2.50. Charlotte: Charlotte Medical Press, 1941.

This volume admirably fulfills the promise made in the preface: "It sets forth in orderly sequence those technics and procedures essential in the training of students for the practice of medicine." It is also a valuable handy reference for those practitioners of medicine—who should continue to be students—who want to refresh their memories on laboratory technique. The directions given for the various procedures used in bacteriology are very clear and explicit.

Unfortunate features of the book are the number of typographical errors that were allowed to creep into it, and the incompleteness of the index. Doubtless these will be corrected in future editions.

Electrotherapy and Light Therapy With the Essentials of Hydrotherapy and Mechanotherapy. By Richard Kovacs, M. D., Professor of Physical Therapy, New York Polyclinic Medical School and Hospital. Ed. 4. 735 pp., illustrated with 314 engravings and a color plate. Price, $8.00. Philadelphia: Lea and Febiger, 1942.

Physical therapeutics has attained the rank of an important medical specialty. Advances in physics have placed in the hand of the physician apparatus with which electrical and radiant energy may be applied to the tissues with effects which frequently surpass those attainable by the use of drugs. Dr. Kovacs, in the present revised edition of his book, discusses exhaustively yet clearly the physics of electric and radiant energy and the application of these forces in the diagnosis and treatment of disease. Hydrotherapy and the various other forms of physical therapy are also discussed in detail. The book can be recommended not only as an essential for the specialist in physicotherapy but also to the general internist and surgeon, who will find a multitude of measures described which are applicable to his own patients.

A Manual of Endocrine Therapy. By Bernard L. Cinberg, M. D., Lecturer in Obstetrics, New York Polyclinic Medical School and Hospital, 178 pages. Price, $3.25. Brooklyn: Chemical Publishing Co., Inc., 1942.

This brief manual was intended as a compendium on the practical aspects of endocrinology. It considers seriatim the various hormones and conditions in which their use has been advocated. Although manifesting a higher degree of discrimination and critique than are found in the average textbook of clinical endocrinology, the book cannot be recommended for the use of the general practitioner. It is impossible to specify certain hormones for a given symptom. Intelligent use of endocrine products requires more than a tabulation of diseases, symptoms and dosages. There is no short cut to good practice in endocrinology, and until the general practitioner appreciates the need for fundamental sound knowledge in this field and ceases to depend on commercial advertisements or brief compendia for his information, practice in this field must remain on a poor level.

Rabies. By Leslie T. Webster, M. D., The Rockefeller Institute for Medical Research, New York. 168 pages, illustrated. Price, $1.75. New York: The Macmillan Company, 1942.

This small volume has been written by a research man to give information primarily to the laity and secondarily to physicians and public health officials on a subject about which rumor, speculation and folklore have obscured facts. The pertinent literature has been examined and a bibliography is included. The appendix is composed of excerpts from the sanitary code of New York City and the State of New Jersey covering the confinement, disposal, and licensing of dogs.

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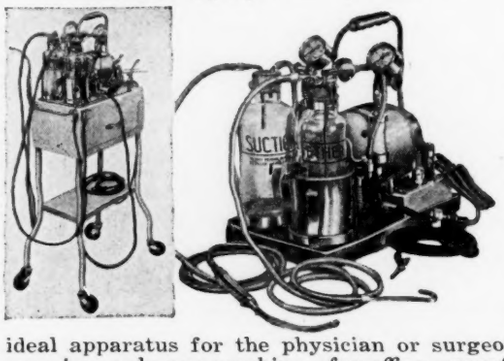

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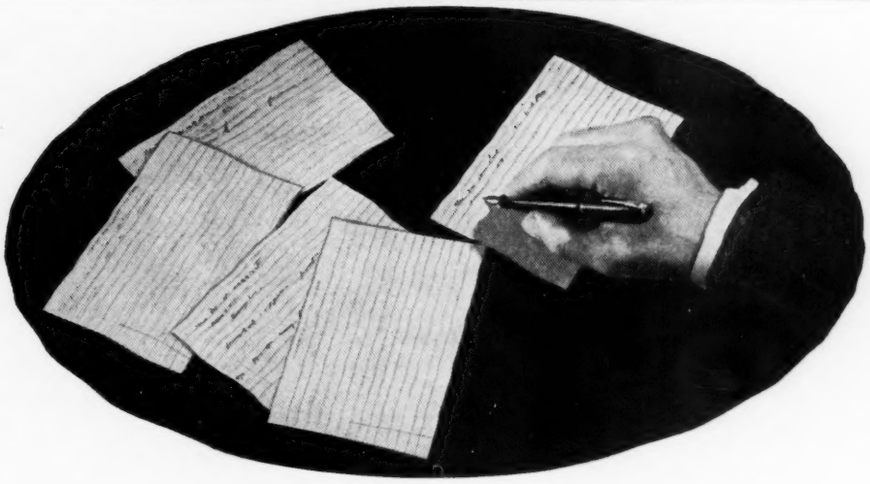

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**J.A.M.A., 93:1110—October 12, 1929*
Brückner, H.—Die Biochemie des Tabaks, 1936

***The Military Surgeon, Vol. 89, No. 1, p. 5, July, 1941*

****ibid. p. 5*

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